

Devi, S.  
09/15/2009

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Set Items Description

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Set	Items	Description
S1	55466	FUSION(S) (PROTEIN? ? OR POLYPROTEIN? ? OR PEPTIDE? ? OR POLYPEPTIDE? ?)
S2	14006	STREPTOCOCC? (3N) ((TYPE OR CLASS OR GROUP) (W)A) OR (STREPTOCOC? OR PEP) (W)M OR PEPM OR M5 OR SM5 OR M24 OR IMMUNOGEN? (W-) PEPTIDE? ?
S3	262	S1 AND S2
S4	123	S3 AND RECOMBINAN?
S6	85	S4/TI,DE,MAJ

-key terms

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7/3,AB/1 (Item 1 from file: 35)

DIALOG(R)File 35:Dissertation Abstracts Online  
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01752242 AADAAIC801250

Design, selection and production of "recombinant"\*\* proteins for prevention of infectious diseases

Author: Hanssom, Marianne

Degree: Dr.Techn.

Year: 1998

Corporate Source/Institution: Kungliga Tekniska Hogskolan (Sweden) (1022  
 )

Source: VOLUME 61/01-C OF DISSERTATION ABSTRACTS INTERNATIONAL.

PAGE 194. 100 PAGES

The development of subunit vaccines is presently one of the main strategies for the generation of new vaccines against infectious diseases. The use of recombinant DNA techniques has facilitated the development of new strategies for construction and production of subunit vaccines. This thesis describes various such techniques, including (i) new general methods for gene assembly applied to antigen-encoding genes, (ii) a suggested strategy for bioprocess improvement applied to the production of a malaria vaccine candidate, (iii) the development of novel live bacterial vaccine delivery systems, based on non-pathogenic staphylococci, and (iv) the *in vitro* selection of a new type of antigen-binding protein.

Two different strategies for *de novo* gene assembly have been developed. A method for assembly and polymerization of DNA fragments was developed, based on the class-IIIS restriction enzyme *Bsp*MI. The central and the C-terminal repeat regions of the *Plasmodium falciparum* malaria blood-stage antigen Pf155/RESA were both polymerized separately (designated M5 and M3, respectively), using this method. Three copies of a respiratory syncytial virus (RSV) G protein encoding fragment (designated G3) was also assembled using this method. For assembly of the *P. falciparum* blood-stage antigen Ag332 repeat region, a solid-phase gene construction method was developed.

Expanded bed adsorption was, for the first time for a recombinant product, used to recover the secreted ZZ-M5 fusion protein directly from crude *E. coli* culture medium by anion-exchange chromatography. The study demonstrated that the initial genetic design can allow integration of unit operations and thus improve the downstream production process.

In the context of live bacterial vaccine delivery, two different non-pathogenic food grade staphylococci, *Staphylococcus*

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*xylosus* and *S. carnosus*, have been investigated, and expression systems allowing efficient surface display of foreign antigenic determinants have been described. New techniques to verify exposure of the recombinant proteins on the bacterial surface were also developed.

Using phage-display technology, a binding protein (affibody) capable of specific recognition of an RSV vaccine candidate was selected *in vitro*. Biopanning of a phage-displayed combinatorial library resulted in the isolation of an affibody, Z<sub>RSV1</sub>, recognizing the G proteins of both subgroup A and B RSV. The potential use of affibodies as diagnostic tools or devices for passive-vaccination applications, is discussed. (Abstract shortened by UMI.)

7/3,AB/2 (Item 2 from file: 35)  
DIALOG(R)File 35:Dissertation Abstracts Online  
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01432783 AADAAI9532069  
AN ASSESSMENT OF PLASMINOGEN ACTIVATION USING GENETICALLY ALTERED FORMS OF  
\*RECOMBINANT\*\*\* STREPTOKINASE (PROTEASES)  
Author: LIZANO-GONZALEZ, SERGIO AGUSTIN  
Degree: PH.D.  
Year: 1995  
Corporate Source/Institution: LOUISIANA STATE UNIVERSITY MEDICAL CENTER  
AT NEW ORLEANS (0854)  
Source: VOLUME 56/05-B OF DISSERTATION ABSTRACTS INTERNATIONAL.  
PAGE 2472. 223 PAGES

Streptokinase is a protein secreted by most group A, C, and G streptococci. Streptokinases interact with the zymogen, plasminogen, to convert it to the enzymatically active form, plasmin. On account of the central role of the plasminogen-plasmin system in regulating key physiological processes which include fibrinolysis and inflammation, streptokinase has been the focus of attention in fibrinolytic therapy as well as a potential pathogenic factor in streptococcal infections. Unlike other plasminogen activators, streptokinase triggers a non-proteolytic activation of plasminogen by forming a stoichiometric complex with plasminogen. This complex develops proteolytic activity and is capable of converting free plasminogen to plasmin. Although numerous studies have focused on this activation mechanism, little is known on the tertiary structure of streptokinase and how it interacts with plasminogen to form the activator complex. A molecular approach was applied to address this question by studying the formation of streptokinase-plasminogen complexes on a solid phase and by constructing genetic variants of the streptokinase molecule using recombinant DNA technology. Streptokinase immobilized on affinity matrices via its NH<sub>2</sub>-terminal fusion to glutathione-S-transferase or by incorporation of a COOH-terminal

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poly-histidine "tail" formed active, nonfragmented complexes with plasminogen; this provided an alternative approach to analyze the complex prior to proteolytic degradation. The activation studies utilizing streptokinase constructs lacking either conserved or highly polymorphic regions of streptokinase suggested that residues in the NH\$\\sb2\$- and the COOH-terminal conserved domains bind plasminogen independently, yet both must be simultaneously present to achieve a fully active complex with plasminogen. This suggests that activation may involve structural complementation between streptokinase and plasminogen, a mechanism previously proposed based on partial homology between streptokinase and certain trypsin-type proteases. On the other hand, an internal 74 amino acid variable domain implicated as a marker for certain streptokinases associated with poststreptococcal glomerulonephritis is non-essential for plasminogen activation. Moreover, mutagenesis studies of glycine-24 of streptokinase previously reported to be indispensable to attain an active complex with plasminogen indicated that this residue is also non-essential for activation. These results may open possibilities for future efforts to characterize the structure/function relationship of streptokinase; such studies may contribute to a better understanding of this important protein interaction and perhaps influence the engineering of streptokinase to improve its therapeutic potential as well as explain its role in streptococcal disease.

7/3,AB/3 (Item 1 from file: 144)  
DIALOG(R)File 144:Pascal  
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14957604 PASCAL No.: 01-0110121  
Removal of amphipathic epitopes from genetically engineered antibodies :  
Production of modified immunoglobulins with reduced immunogenicity  
MATEO Cristina; LOMBARDERO Josefa; MORENO Ernesto; MORALES Alejo; BOMBINO  
Gumersinda; COLOMA Josefina; WIMS Letitia; MORRISON Sherie L; PEREZ Rolando  
Center of Molecular Immunology, P.O. Box 16040, Havana 11600, Cuba;  
Department of Microbiology and Molecular Genetics, UCLA, Los Angeles, CA  
90024, United States

Journal: Hybridoma, 2000, 19 (6) 463-471

Language: English

Several approaches have been developed to reduce the human immune response to nonhuman antibodies. However, chimeric antibodies and humanized antibodies often have decreased binding affinity. We described a new approach for reducing the immunogenicity of chimeric antibodies while maintaining the affinity. This approach seeks to prevent the recognition of murine immunogenic peptides from the antibody variable region by human lymphocytes. Putative immunogenic epitopes in the variable region are identified and subjected to site directed mutagenesis to make them human and/or to break the amphipathic motifs. The R3 antibody, which blocks the epidermal growth factor (EGF) receptor, was used as a model system to test

this approach. Four segments containing possible amphipathic epitopes were found in the heavy variable domain using the program AMPHI. Six amino acids within two of these segments were substituted by the corresponding residues from a homologous human sequence. No mutations were made in the murine light variable domain. Experiments in monkeys suggested that the "detope" R3 antibody was less immunogenic than its chimeric analogue. A search for possible amphipathic epitopes in the Kabat database revealed the presence of conserved patterns in the different families of variable region sequences, suggesting that the proposed method may be of general applicability.

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7/3,AB/4 (Item 2 from file: 144)  
 DIALOG(R)File 144:Pascal  
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14703870 PASCAL No.: 00-0379239  
 Improved systems for hydrophobic tagging of \*recombinant\*\*\* immunogens  
 for efficient iscom incorporation

ANDERSSON C; SANDBERG L; WERNERUS H; JOHANSSON M; LOEVGREN-BENGTSSON K;  
 STAHL S

Department of Biotechnology, Kungliga Tekniska Hoegskolan, 100 44  
 Stockholm, Sweden; Department of Veterinary Microbiology, Division of  
 Virology, Swedish University of Agricultural Sciences, 751 23 Uppsala,  
 Sweden

Journal: Journal of immunological methods, 2000, 238 (1-2) 181-193

Language: English

We have previously reported a strategy for production in *Escherichia coli* of recombinant immunogens fused to a hydrophobic tag to improve their capacity to associate with an adjuvant formulation (Andersson et al., J. Immunol. Methods 222 (1999) 171). Here, we describe a further development of the previous strategy and present significant improvements. In the novel system, the target immunogen is produced with an N-terminal affinity tag suitable for affinity purification, and a C-terminal hydrophobic tag, which should enable association through hydrophobic interactions of the immunogen with an adjuvant system, here being immunostimulating complexes (iscoms). Two different hydrophobic tags were evaluated: (i) a tag denoted M, derived from the membrane-spanning region of *Staphylococcus aureus* protein A (SpA), and (ii) a tag denoted MI consisting of the transmembrane region of hemagglutinin from influenza A virus. Furthermore, two alternative affinity tags were evaluated; the serum albumin-binding protein ABP, derived from streptococcal protein G, and the divalent IgG-binding ZZ-domains derived from SpA. A malaria peptide M5, derived from the central repeat region of the *Plasmodium falciparum* blood-stage antigen Pf155/RESA, served as model immunogen in this study. Four different fusion proteins, ABP-M5-M, ABP-M5-MI, ZZ-M5-M and ZZ-M5-MI, were thus produced, affinity purified and

evaluated in iscom-incorporation experiments. All of the fusion proteins were found in the iscom fractions in analytical ultracentrifugation, indicating iscom incorporation. This was further supported by electron microscopy analysis showing that iscoms were formed. In addition, these iscom preparations were demonstrated to induce M5-specific antibody responses upon immunisation of mice, confirming the successful incorporation into iscoms. The novel system for hydrophobic tagging of immunogens, with optional affinity and hydrophobic tags, gave expression levels that were increased ten to fifty-fold, as compared to the earlier reported system. We believe that the presented strategy would be a convenient way to achieve efficient adjuvant association for recombinant immunogens.

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7/3,AB/5 (Item 3 from file: 144)  
DIALOG(R)File 144:Pascal  
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13931114 PASCAL No.: 99-0113310  
General expression vectors for production of hydrophobically tagged immunogens for direct iscom incorporation

ANDERSSON C; SANDBERG L; MURBY M; SJOELANDER A; LOEVGREN-BENGTSSON K;  
STAHL S

Department of Biotechnology, Kungliga Tekniska Hoegskolan, 100 44  
Stockholm, Sweden; Department of Veterinary Microbiology, Division of  
Virology, National Veterinary Institute, Swedish University of Agricultural  
Sciences, 751 23 Uppsala, Sweden; Department of Veterinary Virology,  
National Veterinary Institute, Swedish University of Agricultural Sciences,  
751 23 Uppsala, Sweden

Journal: Journal of immunological methods, 1999, 222 (1-2) 171-182

Language: English

A new general strategy for the production of recombinant protein immunogens has been investigated. The rationale involves the production of a recombinant immunogen as fused to a composite tag comprising one domain suitable for affinity purification and a hydrophobic tag designed for direct incorporation through hydrophobic interaction of the affinity-purified immunogen into an adjuvant system, in this case immunostimulating complexes (iscoms). Three different hydrophobic tags were evaluated: (i) a tag denoted 1W containing stretches of hydrophobic isoleucine (I) and tryptophan (W) residues; (ii) a tag denoted MI consisting of the transmembrane region of hemagglutinin from influenza A virus; and (iii) a tag denoted PD designed to be pH-dependent in such a way that an amphiphatic alpha -helix would be formed at low pH. As an affinity tag, an IgG-binding domain Z derived from *Staphylococcus aureus* protein A (SpA) was used, and a malaria peptide M5, derived from the central repeat region of the *Plasmodium falciparum* blood-stage antigen Pf155/RESA, served as a model immunogen in this study. Three different fusion proteins,

IW-Z-M5, MI-Z-M5 and PD-Z-M5, were produced in *Escherichia coli*, and after affinity purification these were evaluated in iscom-incorporation experiments. Two of the fusion proteins, IW-Z-M5 and MI-Z-M5 were found in the iscom fraction following preparative ultracentrifugation, indicating iscom incorporation. This was further supported by electron microscopy analysis showing that iscoms were formed. Furthermore, these iscom preparations were demonstrated to induce efficient M5-specific antibody responses upon immunization of mice, confirming successful incorporation into iscoms. The implications of these results for the design and production of subunit vaccines are discussed.

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7/3,AB/6 (Item 4 from file: 144)  
 DIALOG(R)File 144:Pascal  
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12824438 PASCAL No.: 97-0041180  
 Molecular characterization of a major serotype M49 \*group\*\*\* \*A\*\*\*  
 \*streptococcal\*\*\* DNase gene (sdaD)  
 PODBIELSKI A; ZARGES I; FLOSDORFF A; WEBER-HEYNEMANN J  
 Institute of Medical Microbiology, Hospital of the Technical University  
 (Klinikum RWTH), 52057 Aachen, Germany  
 Journal: Infection and immunity, 1996, 64 (12) 5349-5356  
 Language: English  
 Group A streptococci (GAS) express up to four types of secreted DNases. Although GAS infections are correlated with the production of anti-DNase B antibodies, the roles of DNases in the pathogenesis of GAS infections remain unclear. From a lambda library of serotype M49 strain CS101 GAS genome, a 2,147-bp fragment expressing DNase activity on an indicator agar was identified and sequenced. One 1,155-bp open reading frame (ORF) was identified in this fragment. This ORF was found to be 48% identical on the amino acid level to group C streptococcal DNase (Sdc). The regions of highest homology corresponded to amino acid residues that were also identified as part of the active site in staphylococcal nuclease. Transcription analysis revealed a specific 1.3-kb mRNA, which corresponded to the size predicted by the promoter and transcription termination signature sequences and indicated a monocistronic mode of transcription. Allelic replacement of the ORF rendered a M49 mutant devoid of extracellular DNase activity when cultured on indicator agar. Virulence parameters such as resistance to phagocytosis were not affected by the mutation. The sda gene was cloned and expressed in *Escherichia coli* as a thioredoxin fusion. By performing Ouchterlony immunodiffusion on the recombinant protein and by using protein preparations from culture supernatants of wild-type bacteria and the DNase mutant, the results of immunoreactivity with DNase type-specific polyclonal rabbit antisera classified the DNase as a type D enzyme. Fifty percent of patients with

sera exhibiting high titers of antistreptolysin or anti-DNase B antibodies also had SdaD-reactive antibodies in comparison with <10% of serologically normal controls. While the value of recombinant SdaD for diagnostic purposes needs to be clarified, the isogenic DNase mutant pair of M49 should allow the significance of GAS DNase D as a bacterial virulence factor to be determined.

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7/3,AB/7 (Item 5 from file: 144)  
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12551396 PASCAL No.: 96-0231729  
P40, la proteine majeure de la membrane externe de Klebsiella Pneumoniae I-145: clonage, expression de la proteine "recombinante"\*\* et localisation des domaines responsables de l'activite adjuvante  
(P40, the major outer membrane protein of Klebsiella Pneumoniae I-145: clone, expression of the "recombinante"\*\* protein and localisation of the parts involved in the adjuvant activity)

MERLE-POITTE MERLE Christine; AILHAUD G, dir  
Universite de Nice, Nice, Francee  
Univ.: Universite de Nice. Nice. FRA      Degree: Th. doct.  
1995-11; 1995 132 p.

Language: French      Summary Language: French; English  
L'utilisation de molecules peu immunogeniques, peptides ou oligosaccharides, dans l'elaboration de nouveaux vaccins, necessite une association a une proteine porteuse et a un adjuvant pour obtenir une reponse immunologique. P40, l'OmpA de Kelbsiella pneumoniae I-145 presente des proprietes de porteur/adjuvant, demontrées a l'aide de conjugues realises avec differents antigenes: peptides et oligosaccharides. Afin d'utiliser P40 dans la preparation de vaccins, nous avons recherche les sequences impliquees dans l'activite adjuvante de la proteine. Le gene de P40, de 1008 paires de bases, a ete clone et sequence. La proteine recombinante a ete exprimee dans E. coli sous la forme des produits de fusion BBP40 et BBP40G2 triangle C. Ces proteines presentent des proprietes immunologiques analogues a celles de la proteine d'extraction. Pour localiser les sequences responsables du pouvoir adjuvant de P40, trois fragments (1-179, 108-179, 118-179) ont ete clones et exprimes sous la forme BB triangle P40G2 triangle C. Les etudes menees avec ces proteines de fusion ont montre que la partie membranaire rendait compte a elle seule du pouvoir adjuvant de P40. L'antigenicite de la proteine reside au niveau du domaine periplasmique et de la premiere moitie du domaine membranaire. Comme le ciblage de l'antigene sur les cellules presentatrices d'antigene est une facon de potentialiser une reponse immunitaire, nous avons etudie l'interaction de P40 avec une lignee de monocytes-macrophages. L'etude a ete realisee par immunomarquage puis analyse par cytofluorimetrie. P40

interagit directement avec la cellule en se fixant à sa surface. La fixation est rapide. Elle est démontrée sur les macrophages, les splenocytes et les cellules de myélome. L'interaction de P40 avec les monocytes-macrophages se fait par une structure exprimée à la surface des cellules et qui reste à définir. L'identification et l'utilisation des séquences de P40 responsables des propriétés adjuvante et porteuse devraient

7/3,AB/8 (Item 6 from file: 144)  
 DIALOG(R)File 144:Pascal  
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12209620 PASCAL No.: 95-0427390  
 In vitro metabolism of terfenadine by a purified \*recombinant\*\*\*  
 \*fusion\*\*\* \*protein\*\*\* containing cytochrome P4503A4 and NADPH-P450  
 reductase : comparison to human liver microsomes and precision-cut liver  
 tissue slices  
 RODRIGUES A D; MULFORD D J; LEE R D; SURBER B W; KUKULKA M J; FERRERO J L  
 ; THOMAS S B; SHET M S; ESTABROOK R W  
 Abbott Laboratories, Abbott Park IL 60064, USA  
 Journal: Drug metabolism and disposition, 1995, 23 (7) 765-775  
 Language: English

The metabolism of terfenadine was studied with a cDNA-expressed/purified recombinant fusion protein containing human liver microsomal cytochrome P4503A4 (CYP3A4) linked to rat NADPH-P450 reductase (rF450(mHum3A4/mRatOR)L1) and was compared with that observed in the presence of human liver microsomes and precision-cut human liver tissue slices. In all three cases, (<sup>3</sup>H)terfenadine was metabolized to at least three major metabolites. LC/MS (electrospray) analysis confirmed that these metabolites were alpha, alpha-diphenyl-4-piperidinomethanol (M5), t-butyl hydroxy terfenadine (M4), and t-butyl carboxy terfenadine (M3), although the level of M5 detected in the presence of fusion protein was greater than that found with microsomes or tissue slices. Two additional metabolites, M1 (microsomes and tissue slices) and M2 (fusion protein), were also detected, but remain uncharacterized. Consumption of parent drug (microsomes : K<sub>1/2</sub> M = 9.58 +- 2.79 μM, V<sub>max</sub> m<sub>1/2</sub> = 801 +- 78.3 pmol/min/nmol CYP ; fusion protein : K<sub>1/2</sub> M = 14.1 +- 1.13 μM, V<sub>max</sub> m<sub>1/2</sub> = 1670 +- 170 pmol/min/nmol CYP) and t-butyl hydroxylation to M4 (microsomes : K<sub>1/2</sub> M = 12.9 +- 3.74 μM, V<sub>max</sub> m<sub>1/2</sub> = 643 +- 62.5 pmol/min/nmol CYP ; fusion protein : K<sub>1/2</sub> M = 30.0 +- 2.55 μM, V<sub>max</sub> m<sub>1/2</sub> = 1050 +- 141 pmol/min/nmol CYP) obeyed Michaelis-Menten kinetics over the terfenadine concentration range of 1-200 μM. Ketoconazole, a well-documented CYP3A inhibitor, effectively inhibited terfenadine metabolism in all three models. The conversion of M4 to M3, studied with human liver microsomes and fusion protein, was NADPH-dependent and inhibited by ketoconazole. It is concluded that cDNA-expressed CYP3A4, in the form of a NADPH-P450 reductase-linked fusion

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protein, may also serve as a model for studying the metabolism of terfenadine in vitro and many other drugs.

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7/3,AB/9 (Item 7 from file: 144)

DIALOG(R)File 144:Pascal  
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12069531 PASCAL No.: 95-0269829

Oral immunization with the dodecapeptide repeat of the serine-rich Entamoeba histolytica protein (SREHP) fused to the cholera toxin B subunit induces a mucosal and systemic anti-SREHP antibody response

TONGHAI ZHANG; LI E; STANLEY S L JR

Washington univ. school medicine, dep. medicine, St. Louis MO 63110, USA; Washington univ. school medicine, dep. biochemistry molecular biophysics, St. Louis MO 63110, USA; Washington univ. school medicine, dep. molecular microbiology, St. Louis MO 63110, USA

Journal: Infection and immunity, 1995, 63 (4) 1349-1355

Language: English

The intestinal protozoan parasite Entamoeba histolytica causes amebic dysentery, a major cause of morbidity worldwide. The induction of a mucosal antibody response capable of blocking amebic adhesion to intestinal cells could represent an approach to preventing *E. histolytica* infection and disease. Here we describe the expression of a chimeric protein containing an immunogenic dodecapeptide derived from the serine-rich *E. histolytica* protein (SREHP), fused to the cholera toxin B subunit (CtxB). The CtxB-SREHP-12 chimeric protein was purified from *Escherichia coli* lysates and retained the critical G SUB M SUB 1 ganglioside-binding activity of the CtxB moiety. Mice fed the CtxB-SREHP-12 fusion protein along with a subclinical dose of cholera toxin developed mucosal immunoglobulin A -and immunoglobulin G and systemic antibody responses that recognized recombinant and native SRHEP. Our study confirms the feasibility of inducing mucosal immune responses to immunogenicity peptides by their genetic fusion to the CtxB subunit and identifies the CtxB-SREHP-12 chimeric protein as a candidate oral vaccine to prevent *E. histolytica* infection

7/3,AB/10 (Item 8 from file: 144)

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09128233 PASCAL No.: 90-0296613

Immunological properties of hepatitis B core antigen \*fusion\*\*\*  
\*proteins\*\*\*

FRANCIS M J; HASTINGS G Z; BROWN A L; GRACE K G; ROWLANDS D J; BROWN F;  
CLARKE B E

Wellcome Biotechnology Ltd, dep. virology, Beckenham Kent BR3 3BS, United Kingdom

Journal: Proceedings of the National Academy of Sciences of the United States of America (1985), 1990, 87 (7) 2545-2549

Language: English

We demonstrate that rhinovirus peptide-hepatitis B core antigen fusion proteins are 10-fold more immunogenic than peptide coupled to keyhole limpet hemocyanin and 100-fold more immunogenic than uncoupled peptide with an added helper T-cell epitope. The fusion proteins can be readily administered without adjuvant or with adjuvants acceptable for human and veterinary application and can elicit a response after nasal or oral dosing. The fusion proteins can also act as T-cell-independent antigens. These properties provide further support for their suitability as presentation systems for foreign epitopes in the development of vaccines

7/3, AB/11 (Item 1 from file: 440)  
DIALOG(R) File 440: Current Contents Search(R)  
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11629135 GENUINE ARTICLE#: 313EU NUMBER OF REFERENCES: 31  
TITLE: Characterization of the streptococcal C5a peptidase using a C5a-green fluorescent \*protein\*\*\* \*fusion\*\*\* \*protein\*\*\* substrate  
AUTHOR(S): Stafslien DK; Cleary PP (REPRINT)  
AUTHOR(S) E-MAIL: Cleary@lenti.med.umn.edu  
CORPORATE SOURCE: Univ Minnesota, Dept Microbiol, Box 196 FUMC, 420 Delaware St SE/Minneapolis//MN/55455 (REPRINT); Univ Minnesota, Dept Microbiol, /Minneapolis//MN/55455  
PUBLICATION TYPE: JOURNAL  
PUBLICATION: JOURNAL OF BACTERIOLOGY, 2000, V182, N11 (JUN), P3254-3258  
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904  
USA  
ISSN: 0021-9193  
LANGUAGE: English DOCUMENT TYPE: ARTICLE  
ABSTRACT: A glutathione-S-transferase (GST)-C5a-green fluorescent protein (GFP) fusion protein was designed for use as a substrate for the streptococcal C5a peptidase (SCPA). The substrate was immobilized on a glutathione-Sepharose affinity matrix and used to measure wild-type SCPA activity in the range of 0.8 to 800 nM. The results of the assay demonstrated that SCPA is highly heat stable and has optimal activity on the synthetic substrate at or above pH 8.0. SCPA activity was unaffected by 0.1 to 10 mM Ca<sup>2+</sup>, Mg<sup>2+</sup>, and Mn<sup>2+</sup> but was inhibited by the same concentrations of Zn<sup>2+</sup>. The assay shows high sensitivity to ionic strength; NaCl inhibits SCPA cleavage of GST-C5a-GFP in a dose-dependent manner. Based on previously published computer homology modeling, four substitutions were introduced into the putative active site of SCPA: Asp(130)-Ala, His(193)-Ala, Asn(295)-Ala, and Ser(512)-Ala. All four mutant proteins had over 1,000-fold less proteolytic activity on C5a in vitro, as determined both by the GFP assay described here and by a polymorphonuclear cell adherence assay.

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In addition, recombinant SCPA1 and SCPA49, from two distinct lineages of *Streptococcus pyogenes* (group A streptococci), and recombinant SCPB, from *Streptococcus agalactiae* (group B streptococci), were compared in the GFP assay. The three enzymes had similar activities, all cleaving approximately 6 mol of C5a mmol of SCP-1 liter(-1) min(-1).

7/3,AB/12 (Item 2 from file: 440)  
DIALOG(R)File 440:Current Contents Search(R)  
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10942891 GENUINE ARTICLE#: 238YD NUMBER OF REFERENCES: 21  
TITLE: Purification of a biologically active \*recombinant\*\*\* glyceraldehyde 3-phosphate dehydrogenase from *Candida albicans*  
AUTHOR(S): Villamon E; Gozalbo D; Martinez JP; Gil ML (REPRINT)  
AUTHOR(S) E-MAIL: m.luisa.gil@uv.es  
CORPORATE SOURCE: Univ Valencia, Dept Microbial & Ecol, Avda Vicent Andres Estelles S-N/Valencia 46100//Spain/ (REPRINT); Univ Valencia, Dept Microbial & Ecol, /Valencia 46100//Spain/  
PUBLICATION TYPE: JOURNAL  
PUBLICATION: FEMS MICROBIOLOGY LETTERS, 1999, V179, N1 (OCT 1), P61-65  
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ISSN: 0378-1097  
LANGUAGE: English DOCUMENT TYPE: ARTICLE  
ABSTRACT: We report here the purification of a functionally active recombinant glyceraldehyde 3-phosphate dehydrogenase (GAPDH) from *Candida albicans*. The GAPDH protein encoded by the TDH1 gene was obtained as a glutathione S-transferase fusion protein by expression in the vector pGEX-4T-3, and purified by affinity chromatography and thrombin digestion. The purified protein displays GAPDH enzymatic activity (42 mu mol NADH min(-1) mg(-1)) as well as the laminin and fibronectin binding activities previously described. In addition, the recombinant GAPDH is covalently modified by NAD linkage; this modification is stimulated by nitric oxide and probably involves a sulphydryl group (cysteine) residue since it is inhibited by Hg2+ and cysteine. (C) 1999 Published by Elsevier Science B.V. All rights reserved.

7/3,AB/13 (Item 3 from file: 440)  
DIALOG(R)File 440:Current Contents Search(R)  
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10323421 GENUINE ARTICLE#: 170EB NUMBER OF REFERENCES: 53  
TITLE: Characterization of nra, a global negative regulator gene in \*group\*\*\* \*A\*\*\* \*streptococci\*\*\*  
AUTHOR(S): Podbielski A (REPRINT); Woischnik M; Leonard BAB; Schmidt KH  
AUTHOR(S) E-MAIL: andreas.podbielski@medizin.uni-ulm.de

09/151409

CORPORATE SOURCE: Univ Hosp Ulm, Dept Med Microbiol & Hyg, Robert Koch Str 8/D-89081 Ulm//Germany/ (REPRINT); Univ Hosp Ulm, Dept Med Microbiol & Hyg, /D-89081 Ulm//Germany/; Univ Jena, Inst Med Microbiol, /D-07740 Jena//Germany/

PUBLICATION TYPE: JOURNAL

PUBLICATION: MOLECULAR MICROBIOLOGY, 1999, V31, N4 (FEB), P1051-1064

PUBLISHER: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND

ISSN: 0950-382X

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: During sequencing of an 11.5 kb genomic region of a serotype M49 group A streptococcal (GAS) strain, a series of genes were identified including nra (negative regulator of GAS). Transcriptional analysis of the region revealed that nra was primarily monocistronically transcribed. Polycistronic expression was found for the three open reading frames (ORFs) downstream and for the four ORFs upstream of nra. The deduced Nra protein sequence exhibited 62% homology to the GAS RofA positive regulator. In contrast to RofA, Nra was found to be a negative regulator of its own expression and that of the two adjacent operons by analysis of insertional inactivation mutants. By polymerase chain reaction and hybridization assays of 10 different GAS serotypes, the genomic presence of nra, rofA or both was demonstrated. Nra-regulated genes include the fibronectin-binding protein F2 gene (prtF2) and a novel collagen-binding protein (cpa). The Cpa polypeptide was purified as a recombinant maltose-binding protein fusion and shown to bind type I collagen but not fibronectin. In accordance with nra acting as a negative regulator of prfF2 and cpa, levels of attachment of the nra mutant strain to immobilized collagen and fibronectin was increased above wild-type levels. In addition, nra was also found to regulate negatively (four- to 16-fold) the global positive regulator gene, mga. Using a strain carrying a chromosomally integrated duplication of the nra 3' end and an nra-luciferase reporter gene transcriptional fusion, nra expression was observed to reach its maximum during late logarithmic growth phase, while no significant influence of atmospheric conditions could be distinguished clearly.

7/3,AB/14 (Item 4 from file: 440)

DIALOG(R)File 440:Current Contents Search(R)

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07165754 GENUINE ARTICLE#: TX640 NUMBER OF REFERENCES: 30

TITLE: A HOST-VECTOR SYSTEM FOR HETEROLOGOUS GENE EXPRESSION IN STREPTOCOCCUS GORDONII

AUTHOR(S): OGGIONI MR; POZZI G (Reprint)

CORPORATE SOURCE: UNIV SIENA,DIPARTIMENTO BIOL MOLEC,SEZ MICROBIOL,VIA LATERINA 8/I-53100 SIENA//ITALY/ (Reprint); UNIV SIENA,DIPARTIMENTO BIOL MOLEC,SEZ MICROBIOL/I-53100 SIENA//ITALY/; UNIV

09/151409

CAGLIARI, DIPARTIMENTO SCI CHIRURG, SEZ MICROBIOL/CAGLIARI//ITALY/

PUBLICATION: GENE, 1996, V169, N1 (FEB 22), P85-90

ISSN: 0378-1119

LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: We have developed a host-vector system for heterologous gene expression in *Streptococcus gordonii* (Sg) Challis (formerly *Streptococcus sanguis*), a commensal bacterium of the human oral cavity. The system is based on (i) integration of plasmid insertion vectors into the chromosome of specially engineered recipient hosts, and (ii) the use of the M6-protein-encoding gene (emm6) as a partner for construction of translational gene fusions. M6 is a streptococcal surface protein already proven useful as a fusion partner for the delivery of foreign antigens to the surface of Sg [Pozzi et al., Infect. Immun. 60 (1992) 1902-1907]. Insertion vectors carry a drug-resistance marker, different portions of emm6 and a multiple cloning site to allow construction of a variety of emm6-based fusions. Upon transformation of a recipient host with an insertion vector, 100% of transformants acquire both the drug-resistance marker and the capacity of displaying the M6 molecule on the cell surface. Chromosomal integration occurred at high frequency in recipient host GP1221. Transformation with 1 mu g of insertion vector DNA yielded 8.1 x 10(5) transformants per ml of competent cells.

7/3, AB/15 (Item 5 from file: 440)

DIALOG(R) File 440: Current Contents Search(R)

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06636242 GENUINE ARTICLE#: RN224 NUMBER OF REFERENCES: 39

TITLE: CHARACTERIZATION OF A NOVEL FIBRONECTIN-BINDING SURFACE PROTEIN IN

\*GROUP\*\*\* \*A\*\*\* \*STREPTOCOCCI\*\*\*

AUTHOR(S): KREIKEMEYER B; TALAY SR (Reprint); CHHATWAL GS

CORPORATE SOURCE: TECH UNIV CAROLO WILHELMINA BRAUNSCHWEIG, GBF, NATL RES CTR

BIOTECHNOL, DEPT MICROBIOL/BRAUNSCHWEIG//GERMANY/ (Reprint); TECH UNIV

CAROLO WILHELMINA BRAUNSCHWEIG, GBF, NATL RES CTR BIOTECHNOL, DEPT

MICROBIOL/BRAUNSCHWEIG//GERMANY/

PUBLICATION: MOLECULAR MICROBIOLOGY, 1995, V17, N1 (JUL), P137-145

ISSN: 0950-382X

LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: *Streptococcus pyogenes* interacts with host fibronectin via distinct surface components. One of these components is the SfbI protein (streptococcal fibronectin-binding protein, now specified as class I), an adhesin that represents a protein family with characteristic features. Here we present the complete structure of a novel fibronectin-binding protein of *S. pyogenes*, designated SfbII, which is distinct from the previously described SfbI proteins. The sfbII gene originated from a lambda EMBL3 library of chromosomal DNA from group A streptococcal strain A75 and coded for a 113 kDa protein

exhibiting features of membrane-anchored surface proteins of Gram-positive cocci. The expression of biologically active fusion proteins allowed the determination of the location of the fibronectin-binding domain within the C-terminal part of the protein. It consisted of two and a half repeats which share common motifs with fibronectin-binding repeats of other streptococcal and staphylococcal proteins. Purified recombinant fusion protein containing this domain competitively inhibited the binding of fibronectin to the parental *S. pyogenes* strain. Furthermore, polyclonal antibodies against the binding domain specifically blocked the SfbII receptor site on the streptococcal surface. No cross-reactivity could be detected between anti-SfbII antibodies and the sfbI gene product, and vice versa, indicating that the two proteins do not share common immunogenic epitopes. Southern hybridization experiments performed with specific sfbII gene probes revealed the presence of the sfbII gene in more than 55% of 93 streptococcal isolates tested. The majority of the strains also harboured the sfbI gene, and 86% carried at least one of the two sfb genes.

7/3,AB/16 (Item 6 from file: 440)  
 DIALOG(R)File 440:Current Contents Search(R)  
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06288710 GENUINE ARTICLE#: QP912 NUMBER OF REFERENCES: 12  
 TITLE: INTRANASAL IMMUNIZATION WITH \*RECOMBINANT\*\*\* \*GROUP\*\*\* A  
 \*STREPTOCOCCAL\*\*\* \*M\*\*\* PROTEIN FRAGMENT FUSED TO THE B SUBUNIT OF  
 ESCHERICHIA COLI LABILE TOXIN PROTECTS MICE AGAINST SYSTEMIC CHALLENGE  
 INFECTIONS

AUTHOR(S): DALE JB; CHIANG EC  
 CORPORATE SOURCE: DEPT VET AFFAIRS MED CTR, 1030 JEFFERSON  
 AVE/MEMPHIS//TN/38104 (Reprint); UNIV TENNESSEE/MEMPHIS//TN/00000  
 PUBLICATION: JOURNAL OF INFECTIOUS DISEASES, 1995, V171, N4 (APR), P  
 1038-1041

ISSN: 0022-1899

LANGUAGE: ENGLISH DOCUMENT TYPE: NOTE

ABSTRACT: A fusion gene named LT-B-MS was constructed encoding the entire B subunit of *Escherichia coli* labile toxin (LT-B), a 7 amino acid proline-rich linker, and 15 amino-terminal amino acids of type 5 streptococcal M protein. The purified LT-B-MS was immunogenic in rabbits and evoked antibodies against a synthetic peptide copy of the amino-terminus of M5 (SM5[1-15]) and the native M5 protein and opsonic antibodies against type 5 streptococci. The hybrid protein retained the ganglioside-binding activity of LT-B and was tested in mice for its immunogenicity after local administration. Mice that were immunized intranasally with LT-B-MS developed serum antibodies against SM5(1-15) and were significantly protected from death after intraperitoneal challenge infections with type 5 streptococci. The data show that

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protective systemic immune responses may be evoked after intranasal immunization with a fragment of M protein fused to LT-B.

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7/3,AB/17 (Item 7 from file: 440)  
DIALOG(R)File 440:Current Contents Search(R)  
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05692622 GENUINE ARTICLE#: PC836 NUMBER OF REFERENCES: 56  
TITLE: CLONING, SEQUENCING, AND EXPRESSION OF A  
FIBRONECTIN/FIBRINOGEN-BINDING PROTEIN FROM \*GROUP\*\*\* \*A\*\*\*  
\*STREPTOCOCCI\*\*\*  
AUTHOR(S): COURTNEY HS; LI Y; DALE JB; HASTY DL  
CORPORATE SOURCE: VET ADM MED CTR, RES SERV 151,1030 JEFFERSON  
AVE/MEMPHIS//TN/38104 (Reprint); UNIV TENNESSEE, DEPT  
MED/MEMPHIS//TN/38104; UNIV TENNESSEE, DEPT ANAT &  
NEUROBIOL/MEMPHIS//TN/38104  
PUBLICATION: INFECTION AND IMMUNITY, 1994, V62, N9 (SEP), P3937-3946  
ISSN: 0019-9567  
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE  
ABSTRACT: Lipoteichoic acid and several streptococcal proteins have been reported to bind fibronectin (Fn) or fibrinogen (Fgn), which may serve as host receptors. We searched for such proteins by screening a library of genes from M type 5 group A streptococci cloned into Escherichia coli. Lysates of clones were probed with biotinylated Fn and biotinylated Fgn. One clone expressed a 54-kDa protein that reacted with Fn and Fgn. The protein, termed FBP54, was purified and used to immunize rabbits. Anti-FBP54 serum reacted with purified, recombinant FBP54 and with a protein of similar electrophoretic mobility in extracts of M type 5, 6, and 24 streptococci. Anti-FBP54 serum also reacted with 5 of 15 strains of intact, live streptococci, suggesting that PBP54 may be a surface antigen. Southern blot analysis confirmed that the gene is found in group A streptococci but not in *Staphylococcus aureus* or *E. coli*. The cloned gene was sequenced and contained an open reading frame encoding a protein with a calculated molecular weight of 54,186. Partial amino acid sequencing of purified FBP54 confirmed that this open reading frame encoded the protein. As determined by utilizing fusion proteins containing truncated forms of FBP54, the primary Fn/Fgn-binding domain appears to be contained in residues 1 to 89. These data suggest that FBP54 may be a surface protein of streptococci that reacts with both Fn and Fgn and therefore may participate in the adhesion of group A streptococci to host cells.

7/3,AB/18 (Item 8 from file: 440)  
DIALOG(R)File 440:Current Contents Search(R)  
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09/151409

05386116 GENUINE ARTICLE#: NH313 NUMBER OF REFERENCES: 34

TITLE: LOCALIZATION OF IMMUNOGLOBULIN A-BINDING SITES WITHIN M OR M-LIKE PROTEINS OF \*GROUP\*\*\* \*A\*\*\* \*STREPTOCOCCI\*\*\*

AUTHOR(S): BESSEN DE

CORPORATE SOURCE: YALE UNIV, SCH MED, DEPT EPIDEMIOL & PUBL HLTH, MICROBIOL SECT, EPIDEMIOL & PUBL HLTH LAB/NEW HAVEN//CT/06510 (Reprint)

PUBLICATION: INFECTION AND IMMUNITY, 1994, V62, N5 (MAY), P1968-1974

ISSN: 0019-9567

LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Many strains of group A streptococci are capable of binding human immunoglobulin A (IgA) by a nonimmune mechanism. M or M-like proteins constitute a family of structurally diverse molecules which form surface fibrillae, and some of the M or M-like protein forms are responsible for the IgA-binding activity. In this report, the binding site for IgA is localized within two structurally distinct M or M-like proteins, ML2.2 and Arp4. Apart from those structural domains which are common to all M and M-like proteins, ML2.2 and Arp4 lack significant levels of amino acid sequence homology, with the exception of a short segment (ALXGENX DLR) located at residues 21 to 30 of the mature ML2.2 protein. Recombinant fusion polypeptides containing portions of the ML2.2 and Arp4 proteins were expressed in Escherichia coli and tested for binding of human myeloma IgA. A 58-residue polypeptide containing residues 14 to 71 of ML2.2 bound human IgA. The IgA-binding site of Arp4 could be localized to a 53-residue polypeptide containing residues 43 to 95, which encompasses the ALXGENXDLR consensus sequence of Arp4 positioned at residues 50 to 59. Site-specific mutagenesis at three codons within the ALXGENXDLR coding sequence of both the ML2.2 and Arp4 recombinant polypeptides leads to a loss in IgA-binding activity. Thus, the ALXGENXDLR consensus sequence is essential for the nonimmune binding of IgA by both ML2.2 and Arp4. However, the failure to bind IgA by polypeptides which partially overlap the 58- and 53-residue IgA-binding polypeptides of ML2.2 and Arp4, yet contain the ALXGENXDLR consensus sequence, strongly suggests that banking regions are also critical for IgA binding. In summary, the results indicate that common functional domains bearing significant sequence homology are distributed within regions of M or M-like molecules that are otherwise highly divergent.

7/3,AB/19 (Item 9 from file: 440)

DIALOG(R)File 440:Current Contents Search(R)

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03346660 GENUINE ARTICLE#: GX162 NUMBER OF REFERENCES: 36

TITLE: LOCALIZATION OF THE IMMUNOLOGIC ACTIVITY IN THE SUPERANTIGEN STAPHYLOCOCCAL ENTEROTOXIN-B USING TRUNCATED \*RECOMBINANT\*\*\* \*FUSION\*\*\* \*PROTEINS\*\*\*

AUTHOR(S): BUELOW R; OHEHIR RE; SCHREIFELS R; KUMMEREHL TJ; RILEY G; LAMB

Searcher : Shears 308-4994

JR

CORPORATE SOURCE: IMMUNLOG PHARMACEUT CORP, 855 CALIF AVE/PALO ALTO//CA/94304 (Reprint); ST MARYS HOSP, IMPERIAL COLL SCI TECHNOL & MED, SCH MED/LONDON W2 1PG//ENGLAND/

PUBLICATION: JOURNAL OF IMMUNOLOGY, 1992, V148, N1 (JAN 1), P1-6

LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: The exotoxins of certain strains of *Staphylococcus aureus* strains are able both to stimulate potent proliferation and induce anergy in T lymphocytes expressing the appropriate T cell Ag receptor V-beta-gene elements. Although T cell activation by the *S. aureus* enterotoxins requires the presence of accessory cells bearing class II Ag of the MHC, unlike the peptide fragments of nominal Ag, they contact the external surfaces of both the class II MHC and TCR molecules. This paper investigates the immunologically active domains of *S. aureus* enterotoxin B (SEB) using truncated fragments of rSEB expressed as a fusion protein with protein A. The results of the experiments reported here indicate that the minimal fragment of SEB able to stimulate and induce anergy in hemagglutinin-reactive human T cells expressing V-beta-3.1 gene elements is located in the amino-terminal portion of the molecule within residues 1-138. Deletion of the first 30 amino acid residues renders rSEB unable to stimulate T cells expressing V-beta-3.1, whereas polyclonal T cells still respond to this molecule. This implies that the Stimulation of several TCR-V-beta families may be caused by the interaction with different regions of the toxin. The localization of immunologically active sites in the bacterial enterotoxins is needed to investigate both their biology and potential application as immunomodulatory agents.

7/3,AB/20 (Item 1 from file: 357)  
DIALOG(R)File 357:Derwent Biotechnology Abs  
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0258657 DBA Accession No.: 2000-13147 PATENT  
Vaccines for protecting turkeys and pigs against *Erysipelothrix rhusiopathiae* infections comprising a polypeptide sequence from the N-terminal region of an erysipelas protective antigen - \*recombinant\*\*\* vaccine and nucleic acid vaccine to protect pig and turkey from infection

AUTHOR: Fischetti V A; Shimoji Y

CORPORATE SOURCE: New York, NY, USA.

PATENT ASSIGNEE: Univ.New-York-Rockefeller 2000

PATENT NUMBER: WO 200047744 PATENT DATE: 20000817 WPI ACCESSION NO.: 2000-524541 (2047)

PRIORITY APPLIC. NO.: US 119389 APPLIC. DATE: 19990210

NATIONAL APPLIC. NO.: WO 2000US3789 APPLIC. DATE: 20000210

LANGUAGE: English

ABSTRACT: Vaccines containing immunogenic polypeptides (I), or the nucleic

acids (II) that encode them, are claimed. The vaccines comprise immunoprotective groups from the N-terminal region of an erysipelas protective antigen isolated from *Erysipelothrix rhusiopathiae*. Also claimed are: a protein comprising an amino acid sequence corresponding to 25 contiguous amino acids from bases 30-447 of a disclosed 626 amino acid protein sequence; a vaccine comprising an immunogenic protein of *E. rhusiopathiae* and an adjuvant; a nucleic acid encoding the protein antigen; an expression vector containing the nucleic acid; a method for protecting an animal from infection by *E. rhusiopathiae* involving administering (I), (II) and/or an antibody specific for the N-terminal region of erysipelas protective antigen; detecting the presence of protective antibodies to *E. rhusiopathiae* involving detecting antibodies from a sample with (I); and a kit for detecting antibodies to *E. rhusiopathiae*. The vaccines may be used to immunize pigs and turkeys. (I) can be a fusion protein. (61pp)

7/3,AB/21 (Item 2 from file: 357)  
 DIALOG(R) File 357:Derwent Biotechnology Abs  
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0256642 DBA Accession No.: 2000-11132 PATENT  
 Nucleic acids (I) encoding a transforming growth factor beta binding protein, useful for identifying agents for treating osteopenia, osteoporosis and fractures - transforming growth factor-beta binding protein is useful for preventing, treating and diagnosing disease

AUTHOR: Brunkow M E; Galas D J; Kovacevich B; Mulligan J T; Paeper B W;  
 van Ness J; Winkler D G

CORPORATE SOURCE: Cambridge, UK.

PATENT ASSIGNEE: Darwin-Discovery 2000

PATENT NUMBER: WO 200032773 PATENT DATE: 20000608 WPI ACCESSION NO.:  
 2000-412321 (2035)

PRIORITY APPLIC. NO.: US 110283 APPLIC. DATE: 19981127

NATIONAL APPLIC. NO.: WO 99US27990 APPLIC. DATE: 19991124

LANGUAGE: English

ABSTRACT: Isolated nucleic acid (I) encoding a transforming growth factor-beta binding protein (TGF-beta BP) is new and also new is a ribozyme capable of cleaving TGF-beta BP mRNA. Also claimed are: an isolated nucleic acid molecule (I); an isolated oligonucleotide (I'); an isolated protein (II); an expression vector (III) containing a promoter linked to (I); a method (M1) of producing a TGF-beta BP; a host cell (IV) containing (III); an antibody (V) binding (II); a hybridoma (VI) producing (V); a fusion protein (VII); a pair of primers (VIII) amplifying (I); a ribozyme (IX) cleaving RNA; a vector (XI) containing (X); a host cell (XII) containing (X) or (XI); a method (M2) for producing a ribozyme; a method (M3) for increasing bone mineralization; a method (M4) of detecting nucleic acid; a method (M5) for detecting a TGF-beta BP; a non-human transgenic animal (XIII); a

method (M6) for determining candidate molecule; a kit (XIV) for detecting TGF-beta BP expression; and a kit (XV) for detecting TGF-beta BP. (I) and protein (II) are used in the prevention, treatment and diagnosis of diseases associated with inappropriate TGF-beta BP expression, and used in antigen production (157pp)

7/3,AB/22 (Item 3 from file: 357)  
DIALOG(R)File 357:Derwent Biotechnology Abs  
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0243057 DBA Accession No.: 1999-13822  
An antigenic HIV virus-1 peptide sequence engineered into the surface structure of transferrin does not elicit an antibody response - human \*recombinant"\*\* protein and virus peptide conjugate construction and administration to rabbit for use as a \*recombinant"\*\* vaccine

AUTHOR: Ali S A; Joao H C; Hammerschmid F; Eder J; +Steinkasserer A

CORPORATE AFFILIATE: Novartis

CORPORATE SOURCE: Department of Dermatology, University of Erlangen, Hartmannstrasse 14, D-91052 Erlangen, Germany.

email:alexander.steinlasserer@derma.med.uni-erlangen.de

JOURNAL: FEBS Lett. (459, 2, 230-32) 1999

ISSN: 0014-5793 CODEN: FEBLAL

LANGUAGE: English

ABSTRACT: One novel approach for the biological delivery of peptide drugs is to incorporate the sequence of the peptide into the structure of natural transport proteins such as human serum transferrin (HST). There can however be problems with such methods because HST may increase the immunoreactivity of the peptide, in the same way that a carrier protein may be used to produce highly immunogenic peptide haptens. In this study, a recombinant HST carrier protein was constructed which contained the peptide substrate of HIV virus-1 protease. The recombinant HST protein retained its native function and the peptide was surface exposed since it was immunoreactive in native dot blots and it was cleaved by HIV virus-1 protease. The fusion was used to immunize rabbits, but it elicited only a very poor anti-peptide immune response. In contrast to this a strong anti-peptide immune response was raised against both the peptide alone and a chemical conjugate of the peptide with HST. The results obtained suggested that it was possible to attenuate the immune response normally directed against an immunogenic peptide sequence by engineering into a surface exposed loop of HST. (16 ref)

7/3,AB/23 (Item 4 from file: 357)  
DIALOG(R)File 357:Derwent Biotechnology Abs  
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09/151409

0235483 DBA Accession No.: 99-05584 PATENT  
Monoclonal antibody specific for E2A/pbx1 \*fusion\*\*\* \*protein\*\*\* - acute lymphoblastic leukemia-associated \*recombinant\*\*\* \*fusion\*\*\* \*protein\*\*\*-specific monoclonal antibody, used for diagnosis

AUTHOR: Grvenwald S; Sang B

CORPORATE SOURCE: San Diego, CA, USA.

PATENT ASSIGNEE: Pharmingen 1999

PATENT NUMBER: US 5858682 PATENT DATE: 990112 WPI ACCESSION NO.: 99-119870 (9910)

PRIORITY APPLIC. NO.: US 691997 APPLIC. DATE: 960802

NATIONAL APPLIC. NO.: US 691997 APPLIC. DATE: 960802

LANGUAGE: English

ABSTRACT: Monoclonal antibody specific for an E2A/pbx1 fusion protein, where the antibody specifically binds between E2A and pbx1 comprising the sequence SYSVLS but not with the E2A peptide PDSYS, is claimed. Also new are: monoclonal antibody raised against an immunogenic fusion peptide comprising the sequence SYS-VLS/YSV-LS/SVLS (additional sequences may be present at the N-terminus of SYS-VLS, except PD); monoclonal antibody specific for a splice variant E2A/pbx1 fusion protein raised against an immunogenic fusion peptide; monoclonal antibodies produced recombinantly; monoclonal antibody specific for pbx1 and not pbx2 or pbx3, raised against an immunogenic peptide comprising the sequence ATN-VSA-HGS-QAN-SP; hybridoma cell cultures producing any of the above monoclonal antibodies; and a method for detecting acute lymphoblastic leukemia characterized by the presence of as E2A/pbx1 fusion protein. (21pp)

7/3,AB/24 (Item 5 from file: 357)

DIALOG(R) File 357:Derwent Biotechnology Abs

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0227130 DBA Accession No.: 98-08727 PATENT

Virus-like particle useful to treat or prevent microorganism infection - hepatitis D virus \*fusion\*\*\* \*protein\*\*\* production and virus-like particle construction for use in therapy

AUTHOR: Gowans E J; Macnaughton T B

CORPORATE SOURCE: Brisbane, Queensland, Australia.

PATENT ASSIGNEE: Queensland-Dep.Health; Roy.Child.Hosp.Brisbane 1998

PATENT NUMBER: WO 9828004 PATENT DATE: 980702 WPI ACCESSION NO.: 98-377411 (9832)

PRIORITY APPLIC. NO.: AU 964341 APPLIC. DATE: 961224

NATIONAL APPLIC. NO.: WO 97AU884 APPLIC. DATE: 971224

LANGUAGE: English

ABSTRACT: A virus-like particle (VLP) useful for therapy or prevention of at least 1 microorganism infection is claimed. The VLP comprises: at least an antigenic and/or immunogenic polypeptide (or a fragment) from the microorganism fused to at least the last 19 amino acids of the

COOH-terminus of the large protein from hepatitis D virus. The fusion protein produced is at least partially enveloped by hepatitis B virus surface antigen. The VLPs can be combined with a pharmaceutically acceptable adjuvant and used for therapy of patients with at least 1 microorganism infection or to aid in preventing such infections. Because the VLPs contain hepatitis B virus surface antigens, they can be used to stimulate a host's immune system against hepatitis B virus and other microorganisms (bacteria, protozoa and viruses) depending on the protein that is used, preferably from a hepatitis-causing virus. VLPs of disclosed protein sequence are especially claimed. (72pp)

7/3,AB/25 (Item 6 from file: 357)  
DIALOG(R) File 357:Derwent Biotechnology Abs  
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0214322 DBA Accession No.: 97-09443 PATENT  
New \*immunogenic\*\*\* \*polypeptide\*\*\* from Mycoplasma species and related antibodies and nucleic acid - Mycoplasma pneumoniae etc.  
\*recombinant\*\*\* immunogen expression in Escherichia coli or Mycoplasma sp., for use as a \*recombinant\*\*\* vaccine or diagnostic agent, and DNA probe or DNA primer production

AUTHOR: Browning G F; Duffy M F; Whithear K G; Walker I D

CORPORATE SOURCE: Parkville, Victoria, Australia.

PATENT ASSIGNEE: Univ.Melbourne 1997

PATENT NUMBER: WO 9721727 PATENT DATE: 970619 WPI ACCESSION NO.:  
97-332722 (9730)

PRIORITY APPLIC. NO.: AU 957127 APPLIC. DATE: 951213

NATIONAL APPLIC. NO.: WO 96AU803 APPLIC. DATE: 961213

LANGUAGE: English

ABSTRACT: A new recombinant immunogen is derived from a Mycoplasma sp., preferably Mycoplasma pneumoniae, and has a preferred protein sequence, or is a homolog, analog, derivative, variant or mutant. The immunogen is a surface protein with adhesion properties, and has a mol.wt. of 110,000 (SDS-PAGE) or 116,000 (predicted). A derivative with amino acids 9-473, 467-709, 709-850, 846-896, 887-962 or 969-1029, or a fragment with a B-lymphocyte or T-lymphocyte epitope, is also new. A homolog from Mycoplasma penetrans, Mycoplasma iowae, Mycoplasma gallisepticum, Mycoplasma genitalium, Mycoplasma imitans, Mycoplasma muris, Mycoplasma urealyticum or Mycoplasma pirum is also new. The protein may be expressed recombinantly from a virus particle, prokaryote or eukaryote cell, preferably Escherichia coli or a Mycoplasma sp., optionally as a glutathione-transferase (EC-2.5.1.18) fusion protein, for use as a recombinant vaccine against atypical pneumonia, lung lesions and inflammation of the respiratory tract or central nervous system, or as a diagnostic agent. A stringently hybridizing diagnostic DNA probe or DNA primer is also new. (110pp)

7/3,AB/26 (Item 7 from file: 357)  
DIALOG(R) File 357:Derwent Biotechnology Abs  
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0210848 DBA Accession No.: 97-05969 PATENT  
New \*immunogenic"\*\* \*polypeptides"\*\* from *Mycobacterium tuberculosis* and related DNA, vectors etc. - \*recombinant"\*\* immunogen production by vector expression in host cell; application in vaccine generation and tuberculosis diagnosis

AUTHOR: Reed S G; Skeiky Y A; Dillon D C; Campos-Neto A; Houghton R; Vedvick T H; Twardzik D R

CORPORATE SOURCE: Seattle, WA, USA.

PATENT ASSIGNEE: Corixa 1997

PATENT NUMBER: WO 9709428 PATENT DATE: 970313 WPI ACCESSION NO.: 97-192903 (9717)

PRIORITY APPLIC. NO.: US 680574 APPLIC. DATE: 960712

NATIONAL APPLIC. NO.: WO 96US14674 APPLIC. DATE: 960830

LANGUAGE: English

ABSTRACT: Proteins (I) containing an immunogenic part of a soluble *Mycobacterium tuberculosis* antigen (Ag) or its variant differing in conservative substitutions and/or modifications is new and has 1 of 12 specified N-terminal protein sequences. (I) has 1 of about 50 specified DNA sequences, or their complements or sequences that hybridize with them. Also claimed are: a DNA molecule (II) encoding (I); expression vectors containing (II); *Escherichia coli*, yeast or mammal host cells transformed with the vector; a fusion protein (FP) containing one or more (I) or at least one (I) plus ESAT-6. Ags are isolated from *M. tuberculosis* culture fluid or made by expressing DNA. The culture fluid is dialyzed to produce a protein concentrate which is subjected to gel-permeation chromatography on anion-exchange material, eluting the proteins with a salt gradient. These are separated on a Delta-Pak C18 column and tested for their ability to induce T-lymphocyte proliferation. Genomic DNA is isolated by screening a phage lambda library with rabbit or patient antibodies. (I), (II) and FP are useful in vaccines against *M. tuberculosis* and (I) may be used to diagnose tuberculosis. (167pp)

7/3,AB/27 (Item 8 from file: 357)  
DIALOG(R) File 357:Derwent Biotechnology Abs  
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0210809 DBA Accession No.: 97-05930 PATENT  
New \*immunogenic"\*\* \*polypeptides"\*\* from soluble *Mycobacterium tuberculosis* antigens - \*fusion"\*\* \*protein"\*\* gene cloning and expression, and monoclonal antibody, DNA probe and DNA primer production, for use in tuberculosis diagnosis

09/151409

AUTHOR: Reed S G; Skeiky Y A W; Dillon D C; Campos-Neto A; Houghton R;  
Vedwick T H; Twardzik D R

CORPORATE SOURCE: Seattle, WA, USA.

PATENT ASSIGNEE: Corixa 1997

PATENT NUMBER: WO 9709429 PATENT DATE: 970313 WPI ACCESSION NO.:

97-192904 (9717)

PRIORITY APPLIC. NO.: US 680573 APPLIC. DATE: 960712

NATIONAL APPLIC. NO.: WO 96US14675 APPLIC. DATE: 960830

LANGUAGE: English

ABSTRACT: A new *Mycobacterium tuberculosis* 38-kDa antigen or variant has one of several specified N-terminal protein sequences. DNA encoding the protein may be inserted in a vector for expression in an *Escherichia coli*, yeast or mammal host cell. The protein may be used in an immunoassay on a whole blood, serum, plasma, saliva, cerebrospinal fluid or urine sample, to detect *M. tuberculosis* infection. Infection may also be detected by DNA amplification (preferably by polymerase chain reaction) using a specific oligonucleotide DNA primer pair, or by hybridization with a DNA probe. A new monoclonal antibody binding to the protein may also be used as a diagnostic agent. The protein may be expressed as a fusion protein with ESAT-6 (early secretory antigenic target). The products may be used in tuberculosis diagnosis. (189pp)

7/3,AB/28 (Item 9 from file: 357)

DIALOG(R) File 357:Derwent Biotechnology Abs

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0202004 DBA Accession No.: 96-12775 PATENT

Purified and isolated nucleic acid encoding a human 1,4,5-triphosphate receptor/calcium release channel protein - gene cloning and expression using vector; DNA sequence and protein sequence; are used to produce assays for identification/ design of agents which stimulate or suppress the immune system

AUTHOR: Marks A R

CORPORATE SOURCE: New York, NY, USA.

PATENT ASSIGNEE: Mount-Sinai-Sch.Med.; Univ.New-York 1996

PATENT NUMBER: WO 9624846 PATENT DATE: 960815 WPI ACCESSION NO.:

96-393018 (9639)

PRIORITY APPLIC. NO.: US 386039 APPLIC. DATE: 950209

NATIONAL APPLIC. NO.: WO 96US1735 APPLIC. DATE: 960208

LANGUAGE: English

ABSTRACT: A purified and isolated nucleic acid (I) encoding a human 1,4,5-triphosphate receptor/calcium release channel protein (II) having a specified amino acid sequence of 2713 is claimed. Also claimed are: i. a vector comprising (I) as above in which exon SII is excluded; ii. a host cell containing the above vector; iii. a purified and isolated nucleic acid comprising a portion having a nucleic acid sequence consisting essentially of a sequence of 8791 bp; iv. a vector

comprising the nucleic acid of (iii.) and a host cell containing this vector; v. a purified and isolated (II) having a sequence of 2713 amino acids; vi. a fusion protein comprising the (II); vii. an immunogenic peptide fragment of (II) having an amino acid sequence comprising the sequence (Cys)-Glu-Gln-Asn-Glu-Leu-Arg-Asn-Leu-Gln-Glu-Lys-Leu; and viii. a purified antibody which specifically binds to a (II). In (I) exon SII is excluded and (I) is DNA or RNA. Because of the role of (II) in T-lymphocyte activation the methods may be used to identify agents which either block or enhance the ability of (II) to act as a calcium channel. (57pp)

7/3,AB/29 (Item 10 from file: 357)  
DIALOG(R) File 357:Derwent Biotechnology Abs  
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0185107 DBA Accession No.: 95-11928 PATENT  
Site-directed mutagenesis of surface-exposed amino acids of domains of natural bacterial receptors - Staphylococcus or Streptococcus receptor protein engineering and peptide library phage display or bacterium cell surface display, for use as a diagnostic or in therapy

AUTHOR: Nilsson B; Nygren P A; Uhlen M

PATENT ASSIGNEE: Pharmacia 1995

PATENT NUMBER: WO 9519374 PATENT DATE: 950720 WPI ACCESSION NO.: 95-263830 (9534)

PRIORITY APPLIC. NO.: SE 9488 APPLIC. DATE: 940114

NATIONAL APPLIC. NO.: WO 95SE34 APPLIC. DATE: 950116

LANGUAGE: English

ABSTRACT: A novel protein may be obtained by mutagenesis of surface-exposed amino acids of domains of a natural bacterial receptor, without loss of structure and stability. The protein is produced using site-directed mutagenesis, and is selected from a peptide library repertoire based on interaction with human somatotropin, Factor-VIII, insulin, apolipoprotein, biotin, a virus coat protein, a bacterium antigen or a cell marker (CD34 or CD4). The receptor may be from Staphylococcus aureus, Streptococcus pyogenes group-A, Streptococcus sp. group-C,G,L or group-A,C,G, Streptococcus zooepidemicus S212, Peptostreptococcus magnus or Streptococcus agalactiae group-B. The receptor may originate from protein-A or protein-G, or Fc IgG receptor type-I, -II, -III, -IV, -V, -VI, fibronectin receptor, M-protein, plasmin receptor, collagen receptor, fibrinogen receptor, protein-L, protein-H, protein-B or protein-Arp. The protein repertoire may be displayed on a phage or bacterium surface, e.g. as a repressor protein or anchor domain fusion protein, and screened by panning. The products are useful e.g. as diagnostics or in therapy. (55pp)

7/3,AB/30 (Item 11 from file: 357)

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DIALOG(R) File 357:Derwent Biotechnology Abs  
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0181493 DBA Accession No.: 95-05710

Oral immunization with the dodecapeptide repeat of the serine-rich Entamoeba histolytica protein (SREHP) fused to the cholera toxin B-subunit induces a mucosal and systemic anti-SREHP antibody response - candidate oral vaccine to prevent E. histolytica infection

AUTHOR: Zhang T; Li E; +Stanley Jr S L

CORPORATE AFFILIATE: Univ.Washington-St.Louis

CORPORATE SOURCE: Department of Medicine, Washington University School of Medicine, St. Louis, Missouri 63110, USA.

JOURNAL: Infect.Immun. (63, 4, 1349-55) 1995

ISSN: 0019-9567 CODEN: INFIBR

LANGUAGE: English

ABSTRACT: The induction of a mucosal antibody response capable of blocking amebic adhesion to intestinal cells could represent an approach to preventing Entamoeba histolytica infection and disease. The expression is described of a chimeric protein containing an immunogenic dodecapeptide derived from the serine-rich E. histolytica protein (SREHP), fused to the cholera toxin B-subunit (CtxB). The CtxB-SREHP-12 chimeric protein was purified from IPTG-induced Escherichia coli HB101 (plasmid pVA-II/CtxB-SREHP-12) osmotic shock lysates by high-speed centrifugation. The fusion protein retained the critical GM1 ganglioside-binding activity of the CtxB moiety. Mice fed the CtxB-SREHP fusion protein along with a subclinical dose of cholera toxic developed mucosal IgA and IgG and systemic antibody responses that recognized recombinant and native SREHP. The results confirm the feasibility of inducing mucosal immune responses to immunogenic peptides by their genetic fusion to the CtxB subunit and identified the CtxB-SREHP-12 chimeric protein as a candidate oral vaccine to prevent E. histolytica infection. (39 ref)

7/3,AB/31 (Item 12 from file: 357)

DIALOG(R) File 357:Derwent Biotechnology Abs  
(c) 2001 Derwent Publ Ltd. All rts. reserv.

0164199 DBA Accession No.: 94-06750 PATENT

New \*recombinant"\*\* hybrid \*Streptococcus"\*\* \*M"\*\*-protein antigen - Escherichia coli labile toxin, C-repeat or C-terminal fragment \*fusion"\*\* \*protein"\*\* production in non-cariogenic Streptococcus mutans for use as a live \*recombinant"\*\* vaccine

PATENT ASSIGNEE: Univ.Tennessee-Res.Corp. 1994

PATENT NUMBER: WO 9406465 PATENT DATE: 940331 WPI ACCESSION NO.: 94-118162 (9414)

PRIORITY APPLIC. NO.: US 945860 APPLIC. DATE: 920916

NATIONAL APPLIC. NO.: WO 93US8704 APPLIC. DATE: 930915

Searcher : Shears 308-4994

LANGUAGE: English

ABSTRACT: A new immunogenic recombinant multivalent hybrid M-protein comprises fragments of a group-A Streptococcus M-protein carrying epitopes that elicit opsonic and mucosal antibodies against the same serotype, and does not elicit cross-reactive antibodies to mammal heart tissue antigens. The protein may also contain N-terminal portions of different serotypes, particularly M24, of potentially rheumatogenic streptococci. The antigen is preferably M5-protein. The protein may contain the B-subunit of an Escherichia coli labile toxin, C-repeats or a C-terminal fragment of the M-protein, and the fragments may be fused via an amino acid linker (preferably Pro-Gly-Asn-Pro-Ala-Val-Pro or His-Gly). A new recombinant hybrid gene encodes a recombinant M-protein fusion protein. The recombinant M-protein may be produced in a bacterium, e.g. non-cariogenic Streptococcus mutans, using a plasmid vector. The protein may be used as a broad-spectrum recombinant vaccine for protective immunization against group-A rheumatogenic streptococci. (45pp)

7/3,AB/32 (Item 13 from file: 357)

DIALOG(R) File 357:Derwent Biotechnology Abs  
(c) 2001 Derwent Publ Ltd. All rts. reserv.

0158838 DBA Accession No.: 94-01389 PATENT

Synthetic peptide - \*recombinant\*\*\* \*fusion\*\*\* \*protein\*\*\* containing at least one B-lymphocyte and one T-lymphocyte epitope from Streptococcus sp. M-\*protein\*\*\* and useful in streptococcal disease \*recombinant\*\*\* vaccine

PATENT ASSIGNEE: Counc.Queensland-Inst.Med.Res. 1993

PATENT NUMBER: WO 9321220 PATENT DATE: 931028 WPI ACCESSION NO.: 93-351655 (9344)

PRIORITY APPLIC. NO.: AU 921800 APPLIC. DATE: 920408

NATIONAL APPLIC. NO.: WO 93AU131 APPLIC. DATE: 930330

LANGUAGE: English

ABSTRACT: A new synthetic peptide (A) comprising 1 B-lymphocyte epitope from the C-terminus of M protein of group A beta-hemolytic streptococci, may also be produced by recombinant methods. An antibody specific for the B-lymphocyte epitope is only minimally reactive with human heart tissue. Also new are: (1) a vaccine for developing humoral immunity to M protein comprising (A); and (2) an antibody capable of binding to (A). (A) is preferably the T-lymphocyte epitope from the C-terminus of M protein and/or from an extraneous part of, or fusion protein with (A). (A) comprises an N-terminal sequence derived from the conserved region of the M protein (residues 337-492 of type 5 M protein) or single or multiple amino acid substitutions, deletions and/or additions or chemical analogs. (A) preferably has the sequence LRRDLDASREAKKQVEKALE. The T-lymphocyte epitope is from the C-terminus of M protein or an extraneous part of, or fusion protein with (A). (A)

is useful in a vaccine composition for immunizing humans against streptococcal infections and the antibody is useful for infection diagnosis. (57pp)

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7/3,AB/33 (Item 14 from file: 357)  
DIALOG(R)File 357:Derwent Biotechnology Abs  
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0134887 DBA Accession No.: 92-07379 PATENT  
Purified Vibrio cholerae polypeptide - toxin coregulated pilus TcpA gene  
cloning and expression in e.g. Escherichia coli for cholera  
\*recombinant\*\*\* vaccine production

PATENT ASSIGNEE: Harvard-College 1992

PATENT NUMBER: US 5098998 PATENT DATE: 920324 WPI ACCESSION NO.:  
92-123439 (9215)

PRIORITY APPLIC. NO.: US 188016 APPLIC. DATE: 880429

NATIONAL APPLIC. NO.: US 188016 APPLIC. DATE: 880429

LANGUAGE: English

ABSTRACT: A new purified protein or peptide contains at least 8 contiguous amino acids of an immunogenic determinant of the toxin coregulated pilus (TcpA pilus) of Vibrio cholerae. In a wider disclosure, a TcpA gene from V. cholerae may be cloned and used in a cholera recombinant vaccine, or peptides may be prepared synthetically. Immunogenic peptides may be identified by preparing non-overlapping or partially overlapping peptides and raising antibodies to these. Peptides which induce antibodies which either react with and inhibit binding of TcpA pili to host cells or protect animals from virulent V. cholerae are then identified. The new vaccines may be used to inhibit adherence to and colonization of the human intestine by V. cholerae. In an example, Escherichia coli recombinants were constructed, with fusion protein genes containing a TcpA pilus structural gene or a synthetic DNA oligonucleotide encoding related peptide sequences and an alkaline phosphatase (EC-3.1.3.1) gene. The fusion proteins were produced in recombinant E. coli and V. cholerae, and reacted with antibodies raised against TcpA pili. (8pp)

7/3,AB/34 (Item 15 from file: 357)  
DIALOG(R)File 357:Derwent Biotechnology Abs  
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0132491 DBA Accession No.: 92-04983 PATENT  
New \*immunogenic\*\*\* \*peptide\*\*\* sequence from Echinococcus granulosus -  
useful in \*recombinant\*\*\* vaccine, diagnosis of hydatidosis; DNA  
sequence, vector, monoclonal antibody, hybridoma

PATENT ASSIGNEE: Inst.Pasteur; Inst.Pasteur-Lille; INSERM 1992

PATENT NUMBER: WO 9201051 PATENT DATE: 920123 WPI ACCESSION NO.:

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92-056866 (9207)

PRIORITY APPLIC. NO.: FR 908900 APPLIC. DATE: 900712

NATIONAL APPLIC. NO.: WO 91FR563 APPLIC. DATE: 910711

LANGUAGE: French

**ABSTRACT:** A new immunogenic peptide sequence (I) from *Echinococcus granulosus* antigen 5 is recognized by sera of hydatidosis patients and by IgG1 monoclonal antibodies (MAbs) produced by hybridoma EG02154/12 (CNCR I-957). Also new are: a DNA sequence encoding (I); plasmids containing the DNA; vectors containing the DNA; hosts transformed with the vectors; MAbs specific for (I); and hybridoma EF02154/12. (I) contains all or part of the disclosed 152- or 37-amino acid (AA) sequences. (I) preferably comprises AA 89-122 EAQKAKTKLEEVRLDLDSDKTKLKN and AKTAEQKAK. (I) can be used for diagnosis of hydatidosis in humans and animals by detection of specific antibodies. (I) can also be used in the construction of vaccines for the prevention and treatment of hydatidosis. Preparation of (I) involved extraction of RNA from protoscolecs of *E. granulosus*, conversion to cDNA and gene bank construction in phage lambda-gt11. 2 Positive clones were identified by screening with sera of infected patients. Phages containing these inserts were transfected into *Escherichia coli* Y1089. Bacterial lysates contained a fusion protein including (I). (56pp)

7/3,AB/35 (Item 16 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs

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0130173 DBA Accession No.: 92-02665 PATENT

New muscarinic receptor "fusion"\*\* "protein"\*\* - used to produce antibody and study receptors

PATENT ASSIGNEE: Nat. Inst. Health-Bethesda 1991

PATENT NUMBER: US 7654971 PATENT DATE: 911112 WPI ACCESSION NO.:

91-368910 (9150)

PRIORITY APPLIC. NO.: US 654971 APPLIC. DATE: 910214

NATIONAL APPLIC. NO.: US 654971 APPLIC. DATE: 910214

LANGUAGE: English

**ABSTRACT:** The following are disclosed: (A) recombinant DNA comprising (a) DNA encoding a region of a cytoplasmic loop of a muscarinic receptor (MR) and (b) a vector for introducing the DNA into host cells; the MR cytoplasmic loop is present in a MR selected from m1, m2, m3, m4 and m5; the cytoplasmic loop is the inner third cytoplasmic loop of the MR or i3; (B) a host cell transformed or transfected with the recombinant DNA molecule in a manner allowing expression of a protein encoded by the recombinant DNA molecule; (C) recombinant fusion proteins consisting of a region of a MR cytoplasmic loop and an amino acid sequence encoded by a parent vector; and (D) antibodies specific for the fusion proteins. Expression plasmids are produced by subcloning DNA encoding unique regions of the inner third (i3) cytoplasmic loops of

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the human MRs m1-m5 and produced by amplification of DNA using the polymerase chain reaction into the parent plasmid pET or plasmid pGEX2T. The fusion proteins and antibodies are used to study structure, function and localization of the MR family in cells and tissues. The plasmids are also used for DNA probe construction. (30pp)

7/3,AB/36 (Item 17 from file: 357)  
DIALOG(R)File 357:Derwent Biotechnology Abs  
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0125291 DBA Accession No.: 91-12933 PATENT  
New fusion plasmid - \*recombinant\*\*\* \*lipoprotein\*\*\* preparation;  
\*lipoprotein\*\*\* signal \*peptide\*\*\* and target \*protein\*\*\* gene  
\*fusion\*\*\* cloning and expression in e.g. Escherichia coli; \*protein\*\*\*  
secretion

PATENT ASSIGNEE: Nat.Res.Counc.Can. 1991

PATENT NUMBER: WO 9109952 PATENT DATE: 910711 WPI ACCESSION NO.:  
91-222904 (9130)

PRIORITY APPLIC. NO.: US 456473 APPLIC. DATE: 891226

NATIONAL APPLIC. NO.: WO 90CA460 APPLIC. DATE: 901227

LANGUAGE: English

ABSTRACT: A fusion plasmid for in vivo biosynthesis of a lipid-modified polypeptide is new. The plasmid contains DNA encoding a lipoprotein signal peptide and at least the 1st amino acid of a mature lipoprotein. DNA encoding a target protein is inserted into the plasmid to produce the lipid-modified recombinant protein. The vector preferably contains DNA encoding a lipoprotein signal peptide, cysteine and a sequence with a B-turn or exogenous protease recognition sequence. The signal peptide contains a positively-charged N-terminal region, a central hydrophobic region and a C-terminal region containing a recognition site for signal peptidase-II. The recombinant fusion protein is also claimed. The fusion plasmid allows production of immunogenic polypeptides as part of recombinant lipopeptides secreted across the cytoplasmic membrane, and recovery from cells. In an example, expression of the lipid-modified peptide from plasmid pkLY4 was studied in Escherichia coli recA lacIq DH5-alpha-F'1Q. Compared to non-induced cells, transformants with plasmid pkLY4 induced with IPTG produced an additional 3H-palmitate-rich substance. (26pp)

7/3,AB/37 (Item 18 from file: 357)  
DIALOG(R)File 357:Derwent Biotechnology Abs  
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0118548 DBA Accession No.: 91-06190 PATENT  
Epitope from HIV virus, SIV virus, HTLV-I virus or HTLV-II virus -  
potential application as \*recombinant\*\*\* vaccine; protein sequence

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PATENT ASSIGNEE: Inst.Pasteur; Univ.Pierre+Marie-Curie 1991

PATENT NUMBER: WO 9102544 PATENT DATE: 910307 WPI ACCESSION NO.:  
91-087117 (9112)

PRIORITY APPLIC. NO.: FR 8911044 APPLIC. DATE: 890818

NATIONAL APPLIC. NO.: WO 90FR620 APPLIC. DATE: 900817

LANGUAGE: French

ABSTRACT: New compositions comprise (a) at least 1 immunogenic peptide containing a B epitope derived from the env glycoprotein of a pathogenic retro virus, and (b) at least 1 T epitope derived from a different protein of the same retro virus, or from a corresponding protein of a different retro virus, where (a) and (b) are preferably linked in the form of at least 1 hybrid molecule e.g. a fusion protein. The retro virus is an immunodeficiency virus, especially HIV virus, SIV virus, HTLV-I virus or HTLV-II virus. Also claimed are recombinant nucleic acid (NA) sequences encoding the hybrid molecules, host cells transformed with the NA sequences, and DNA or RNA sequences coding for (a) and (b). Component (a) comprises at least 1 (preferably all) of the 21 known peptides corresponding to the HIV virus Putney epitope. Component (b) comprises an HIV virus nef or gag protein (e.g. P18 or P25 gag proteins or P27 nef protein) or a fragment of such a protein. The compositions are useful as vaccines against retro virus infections (especially AIDS). The NA sequences are useful as hybridization probes for diagnosis of retro virus infections. (43pp)

7/3,AB/38 (Item 19 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs  
(c) 2001 Derwent Publ Ltd. All rts. reserv.

0114369 DBA Accession No.: 91-02011 PATENT

DNA encoding HSV-2 type glycoprotein-G - herpes simplex virus-2 gene cloning in Escherichia coli; DNA sequence; potential application in \*recombinant\*\* vaccine and diagnostic DNA probe construction

PATENT ASSIGNEE: Triton-Biosciences 1990

PATENT NUMBER: WO 9013652 PATENT DATE: 901115 WPI ACCESSION NO.:  
90-361487 (9048)

PRIORITY APPLIC. NO.: US 351740 APPLIC. DATE: 890512

NATIONAL APPLIC. NO.: WO 90US2639 APPLIC. DATE: 900510

LANGUAGE: English

ABSTRACT: A new recombinant DNA sequence comprises a gene encoding all or part of herpes simplex virus-2 (HSV-2) glycoprotein-G (gG) operably linked to an expression control sequence. The following are also new: a prokaryote (e.g. Escherichia coli JM103, CAG456 or N4830 (preferred), Pseudomonas sp. or Bacillus sp.) or eukaryote (e.g. Saccharomyces cerevisiae, another fungus, or animal, insect or plant cell culture) host transformed with the DNA; purified DNA encoding gG, or homologous sequences; a vector (e.g. plasmid 19gGSE or plasmid trpE/gG) containing the DNA; recombinant HSV-2 gG, in glycosylated or non-glycosylated

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form; an antibody against the protein; and a fusion protein containing gG and a non-immunogenic polypeptide. The antibodies are useful for passive immunization, purification by affinity chromatography, and for HSV-2 diagnosis, e.g. for screening during pregnancy. The proteins are useful for detecting HSV-2 antibodies, and in recombinant vaccine construction. The DNA sequences are useful in DNA probe construction for application in diagnosis. (72pp)

7/3,AB/39 (Item 20 from file: 357)  
DIALOG(R) File 357:Derwent Biotechnology Abs  
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0112523 DBA Accession No.: 91-00165 PATENT  
Protein-E of Haemophilus influenzae or its epitope - \*recombinant\*\*\*  
protein-E production using plasmid pPX525; DNA sequence determination;  
application as vaccine  
PATENT ASSIGNEE: Praxis-Biol. 1990  
PATENT NUMBER: WO 9010458 PATENT DATE: 900920 WPI ACCESSION NO.:  
90-304862 (9040)

PRIORITY APPLIC. NO.: US 320971 APPLIC. DATE: 890309  
NATIONAL APPLIC. NO.: WO 90US1317 APPLIC. DATE: 900309

LANGUAGE: English

ABSTRACT: Pure protein-E of Haemophilus influenzae, or a peptide or protein having an epitope or epitopes of protein-E, is claimed. Protein-E may be purified from H. influenzae or prepared by recombinant DNA techniques. DNA encoding protein-E or fragments may be isolated from a H. influenzae gene bank using a probe based on the amino acid sequence of protein-E. Also claimed are: (i) recombinant protein-E; (ii) specified DNA sequence and protein sequence encoding protein-E; (iii) modified sequences which do not affect the biological properties; (iv) a fusion protein comprising protein-E linked to an antigen of an organism or an epitope; and (v) a recombinant plasmid encoding the fusion protein. The organism in (iv) is a bacterium, virus, parasite, fungus or etiolated agent of otitis media such as Streptococcus pneumoniae, Streptococcus pyogenes group A, Staphylococcus aureus, Branhamella catarrhalis or respiratory-syncytial virus. The plasmid in (v) is plasmid pPX525. The peptides and proteins can be used in univalent or multivalent vaccines. Protein-E can protect against non-typable H. influenzae infection. (86pp)

7/3,AB/40 (Item 21 from file: 357)  
DIALOG(R) File 357:Derwent Biotechnology Abs  
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0110793 DBA Accession No.: 90-13484 PATENT  
Babesia DNA, polypeptides and monoclonal antibodies - Babesia bovis antigen

Searcher : Shears 308-4994

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gene cloning and expression in *Escherichia coli*; monoclonal antibody preparation and hybridoma construction; potential "recombinant"\*\* vaccine construction

PATENT ASSIGNEE: CSIRO 1990

PATENT NUMBER: EP 382012 PATENT DATE: 900816 WPI ACCESSION NO.: 90-247993  
(9033)

PRIORITY APPLIC. NO.: AU 897722 APPLIC. DATE: 891116

NATIONAL APPLIC. NO.: EP 90101488 APPLIC. DATE: 900125

LANGUAGE: English

ABSTRACT: The following are claimed: an antigen inducing protective immunity against challenge with a cattle Babesia spp. (e.g. *Babesia bovis*) which reacts with a monoclonal or polyclonal antibody; a recombinant antigen, which is expressed as a beta-galactosidase (EC-3.2.1.23) or glutathione-transferase (EC-2.5.1.18) fusion protein; a monoclonal antibody (MAb) reactive with an antigen on the surface of Babesia-infected erythrocytes or within a spherical or mitochondria-like organelle; a DNA sequence encoding the antigen, isolated from an infected erythrocyte cDNA or genomic gene bank in *Escherichia coli*, using plasmid pBR322, phage lambda-gt11 or plasmid pGEX1 as expression vector; and a DNA sequence having a repetitive component of unit length 90 bp followed by a unique component of 1414 bp encoding an immunogenic polypeptide. MAb W11C5, obtained from hybridoma 88 121501-W11C5.1 A5.F10.A2 cell culture, and a cDNA insert in plasmid pGEX11C5 corresponding to AGAL deposit 88/39601, are specifically claimed. The antigens are used in recombinant vaccine construction and as diagnostic agents for babesiosis (e.g. tick fever).

(43pp)

7/3,AB/41 (Item 22 from file: 357)

DIALOG(R) File 357:Derwent Biotechnology Abs  
(c) 2001 Derwent Publ Ltd. All rts. reserv.

0084862 DBA Accession No.: 89-02853 PATENT

Monoclonal antibody preparation against HIV virus-1 for AIDS therapy - hybridoma construction

PATENT ASSIGNEE: Tanox-Biosyst.; Baylor-Coll.Med. 1988

PATENT NUMBER: WO 8809181 PATENT DATE: 881201 WPI ACCESSION NO.:  
88-353807 (8849)

PRIORITY APPLIC. NO.: US 197766 APPLIC. DATE: 880523

NATIONAL APPLIC. NO.: WO 88US1797 APPLIC. DATE: 880527

LANGUAGE: English

ABSTRACT: New monoclonal antibodies (MAbs), of mouse IgG or human/mouse type, and their fragments neutralize HIV virus-1 infections, e.g. AIDS and AIDS related complex. The MAb binds the gp120 envelope protein of HIV virus-1 and is BAT085, BAT123, BAT267 or BAT509. Also new are: (1) the MAb-producing hybridomas, prepared by fusing immunized mouse spleen cells with NS-1 myeloma cells; (2) bispecific MAbs comprising 2

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different antigen binding domains, 1 of which is the HIV virus-1 gp120 binding domain; (3) a MAb conjugate which includes a cytotoxic agent, a virucide, or an agent which facilitates passage through a blood-brain barrier; (4) an anti-idiotypic MAb against an HIV virus-1-specific MAb; (5) an immunogenic peptide which neutralizes HIV virus-1; (6) a chimeric virus-neutralizing immunoglobulin which comprises a virus-specific antigen-binding region of non-human origin and a constant region of human origin; (7) a fusion gene encoding a recombinant light or heavy chain immunoglobulin; and (8) an expression vector. The MAbs inhibit infection of T-lymphocytes and prevent the formation of a syncytium. (111pp)

7/3,AB/42 (Item 23 from file: 357)  
DIALOG(R)File 357:Derwent Biotechnology Abs  
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0077559 DBA Accession No.: 88-08408 PATENT  
New conjugates and \*fusion"\*\* \*proteins"\*\* of \*immunogenic"\*\*  
\*polypeptide"\*\* and hepatitis B core antigen - and T-cell stimulating  
polypeptides corresponding to core antigen epitopes, useful as vaccine  
PATENT ASSIGNEE: Scripps 1988  
PATENT NUMBER: EP 271302 PATENT DATE: 880615 WPI ACCESSION NO.: 88-163287  
(8824)  
PRIORITY APPLIC. NO.: US 106538 APPLIC. DATE: 871007  
NATIONAL APPLIC. NO.: EP 87310725 APPLIC. DATE: 871207  
LANGUAGE: English  
ABSTRACT: A new immunogenic polypeptide conjugate (A) comprises hepatitis B virus core antigen (HBcAg) linked through an amino acid residue to a polypeptide immunogen (I). Also new are: (1) immunogenic fusion proteins (II) comprising HBcAg protein peptide-bonded to a pathogen-related (I); (2) T-cell stimulating polypeptides (III) of 15-70 amino acids, corresponding to a part of the core protein from positions 70-140 from the N-terminus; and (3) composite immunogens containing at least 20 amino acid residues and including (III). HBcAg is a core protein in particulate form and (I) is a pathogen-related immunogen, especially hepatitis B surface antigen. Coupling (I) to HBcAg or (III) improves its immunogenicity. (A), (II), (III) and the composite immunogens are useful in vaccines, while (III) can be used therapeutically to improve T-cell response to HBcAg in infected subjects. The fusion proteins are made by DNA recombinant methods while (III) are made by peptide synthesis. (47pp)

7/3,AB/43 (Item 24 from file: 357)  
DIALOG(R)File 357:Derwent Biotechnology Abs  
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0072497 DBA Accession No.: 88-03346 PATENT  
\*Recombinant\*\*\* DNA encoding \*fusion\*\*\* \*protein\*\*\* of Newcastle-disease virus or its \*immunogenic\*\*\* \*polypeptide\*\*\* fragments; useful in fowl vaccine - expression in Escherichia coli or Saccharomyces cerevisiae using plasmid pYDE1 vector

PATENT ASSIGNEE: SK+RIT 1988

PATENT NUMBER: EP 252060 PATENT DATE: 880107 WPI ACCESSION NO.: 88-001887 (8801)

PRIORITY APPLIC. NO.: US 880371 APPLIC. DATE: 860630

NATIONAL APPLIC. NO.: EP 87870091 APPLIC. DATE: 870629

LANGUAGE: French

ABSTRACT: A new recombinant DNA molecule (I) comprises a sequence coding for the fusion protein of Newcastle-disease virus (NDV) or a fragment or derivative of this coding for a polypeptide able to induce an immune response to the fusion protein. Also new are (1) a 1,764 bp DNA sequence coding for NDV fusion protein; (2) vectors expressing the DNA when inserted downstream of a regulatory region in yeast, and (3) microorganisms transformed with this DNA. Vector plasmid pYDE1 is claimed. NDV fusion protein and immunogenic polypeptides are useful in vaccines for protecting fowl against NDV infection, and can also be used diagnostically. Such vaccines can be used without risk of inducing respiratory disorder. Poly(A)-mRNA is isolated from NDV-infected BHK-21 cells, used to construct cDNA, and this is inserted into pBR322. Recombinant plasmids were cloned in Escherichia coli MM 294 and selected by hybridization with a viral RNA probe. The clone II.14(F) containing the longest insert was sequenced; it contains the claimed 1,764 bp sequence encoding a 526 amino acid protein. (21pp)

7/3,AB/44 (Item 25 from file: 357)

DIALOG(R) File 357:Derwent Biotechnology Abs  
(c) 2001 Derwent Publ Ltd. All rts. reserv.

0054042 DBA Accession No.: 86-11890 PATENT

Vaccine for protecting mammals against malaria - comprises \*immunogenic\*\*\* \*polypeptides\*\*\* containing at least 4 tandem repeat units of Plasmodium falciparum circumsporozoite protein

PATENT ASSIGNEE: SK+Beckman; U.S.Secr.Army 1986

PATENT NUMBER: EP 192626 PATENT DATE: 860827 WPI ACCESSION NO.: 86-227171 (8635)

PRIORITY APPLIC. NO.: US 699116 APPLIC. DATE: 850207

NATIONAL APPLIC. NO.: EP 86870014 APPLIC. DATE: 860203

LANGUAGE: English

ABSTRACT: A polypeptide (I) comprising at least 4, and preferably 16-148, tandem repeat units of the Plasmodium falciparum circumsporozoite (CS) protein is used, together with a carrier, for preparing a vaccine for protecting humans against malaria. (I) Preferably comprises Rtet32, RNS1, NS1R, Rtet86, RG, RLA or RN polypeptide, and is particularly

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R32tet32 or R32LA. The *P. falciparum* repeat unit is Asn-Ala-Asn-Pro, but variations are possible provided the reactivity of antibodies is not adversely affected. (I) May be a fusion polypeptide having non-CS protein repeat unit sequences, the non-CS protein being a carrier to enhance immunogenicity or to facilitate cloning and expression in a recombinant microorganism. (I) Are obtained e.g. by DNA chemical synthesis, production of a vector and transformation of *Escherichia coli*. The (I) is then expressed and recovered. (I) Are immunogenic and can confer immunity in mammals to infection by *P. falciparum*, without adverse side effects. (35pp)

7/3,AB/45 (Item 1 from file: 351)

DIALOG(R) File 351:Derwent WPI

(c) 2001 Derwent Info Ltd. All rts. reserv.

013334131

WPI Acc No: 2000-506070/200045

XRAM Acc No: C00-151958

Propagation of adenovirus in a host cell, comprising expressing an artificial "recombinant" receptor on the surface of a host cell and infecting the host with the adenovirus, useful for cell specific gene therapy

Patent Assignee: UAB RES FOUND (UABR-N)

Inventor: CURIEL D T; DMITRIEV I; DOUGLAS J T; KRASNYKH V N

Number of Countries: 021 Number of Patents: 002

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200046364	A1	20000810	WO 2000US2867	A	20000203	200045 B
AU 200028693	A	20000825	AU 200028693	A	20000203	200059

Priority Applications (No Type Date): US 99118880 A 19990205

Patent Details:

Patent No	Kind	Lan Pg	Main IPC	Filing Notes
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WO 200046364 A1 E 49 C12N-015/09

Designated States (National): AU CA JP

Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU

MC NL PT SE

AU 200028693 A C12N-015/09 Based on patent WO 200046364

Abstract (Basic): WO 200046364 A1

Abstract (Basic):

NOVELTY - A method for propagation of adenovirus in a host cell, comprising expressing an artificial recombinant receptor on the surface of a host cell and infecting the host with the adenovirus, is new.

DETAILED DESCRIPTION - A method for propagation of adenovirus in a host cell, comprises expressing an artificial recombinant receptor on the surface of a host cell and infecting the host with the adenovirus.

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The adenovirus infects the host cell independently of the ubiquitous adenovirus fiber protein receptor by interacting with the artificial, recombinant receptor.

INDEPENDENT CLAIMS are also included for the following:

(1) a host cell expressing a recombinant, artificial receptor designed to allow adenovirus propagation; and  
(2) a recombinant adenovirus expressing a novel protein marker for adenovirus propagation using an artificial receptor.

ACTIVITY - None given.

MECHANISM OF ACTION - Gene therapy.

No biological data given.

USE - The adenovirus vector is useful for cell specific gene therapy.

ADVANTAGE - The vectors are specific for certain cell types and eliminate endogenous tropism through modification of the fiber protein by addition of a C-terminal tag.

pp; 49 DwgNo 0/6

7/3,AB/46 (Item 2 from file: 351)  
DIALOG(R) File 351:Derwent WPI  
(c) 2001 Derwent Info Ltd. All rts. reserv.

013023454

WPI Acc No: 2000-195305/200017

XRAM Acc No: C00-060595

XRPX Acc No: N00-144464

New \*immunogenic\*\*\* \*polypeptides\*\*\* useful as a vaccine against Lyme disease and for treating and detecting borrelia infection in mammals consists an epitope of Borrelia burgdorferi OspC fragment

Patent Assignee: GUNDERSEN LUTHERAN MEDICAL FOUND INC (GUND-N)

Inventor: CALLISTER S M; JOBE D A; LOVRICH S D; SCHELL R F; CALLISTER S N

Number of Countries: 086 Number of Patents: 003

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200006745	A1	20000210	WO 99US17270	A	19990730	200017 B
AU 9953282	A	20000221	AU 9953282	A	19990730	200029
US 6210676	B1	20010403	US 9894955	A	19980731	200120
			US 99364083	A	19990730	

Priority Applications (No Type Date): US 9894955 A 19980731; US 99364083 A 19990730

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 200006745 A1 E 51 C12N-015/31

Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK

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SL TJ TM TR TT UA UG US UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR  
IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW

AU 9953282 A C12N-015/31 Based on patent WO 200006745  
US 6210676 B1 A61K-039/02 Provisional application US 9894955

Abstract (Basic): WO 200006745 A1

Abstract (Basic):

NOVELTY - An isolated, immunogenic polypeptide fragment (I) of outer surface protein polypeptide (Osp) C of *Borrelia burgdorferi* comprising an epitope of OspC (an OspC Dra fragment) that comprises residues 145-194 of a 194 amino acid sequence (A) fully defined in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a DNA molecule (II) encoding (I);
- (2) an expression vector comprising (II);
- (3) a kit for diagnosing borrelia infection in mammals, including humans comprising (I) disposed in a suitable container, and instructions for using the kit; and
- (4) detecting borrelia infection in mammals, especially humans comprising:
  - (a) contacting a body fluid of a mammalian host suspected to suffer from borrelia infection with (I); and
  - (b) determining whether (I) is conjugated to antibodies present in the body fluid of the host using an enzyme-linked immunosorbant assay, indicating presence of borrelia infection.

ACTIVITY - Antibacterial; immunomodulatory.

MECHANISM OF ACTION - Vaccine. The biological activity of (I) was determined using mice. The mice were vaccinated with *B. burgdorferi* 50772 and the level of borreliacidal antibodies was determined at various time intervals after vaccination. Borreliacidal activity was detectable after 14 days (20b) after the initial vaccination, and peaked after 56 days (2560).

b=reciprocal of highest serum dilution with significant borreliacidal activity

USE - (I) is used to prevent (vaccinate against), treat or detect *Borrelia* especially *B. burgdorferi* infections (i.e. Lyme disease) in mammals, including humans.

ADVANTAGE - (I) provides for a superior diagnostic antigen that detects early Lyme disease infection, predicts successful eradication of the organism from the host, and discriminates between individuals with Lyme disease and individuals who have been vaccinated with an OspA Lyme disease vaccine. By using the portion of the ospC gene containing borreliacidal epitope, specificity and prognostic potential of diagnostic testing is enhanced without significant loss of sensitivity. Also, vaccination problems are minimized because the other parts of the protein are not present, thus limiting vaccination side-effects and

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making it easier to induce, maintain and monitor the effective protective antibody response. A test which detects borreliacidal antibodies against the borreliacidal epitope of OspA and OspB in addition to OspC would give reduced cross reactivity, increased specificity, greater accuracy and fewer false-positive diagnoses. Detection of anti-OspC borreliacidal antibodies advantageously gives an early diagnosis which anti-OspA and anti-OspB borreliacidal antibodies cannot do. Unlike vaccination with OspA, vaccination with OspC results in clearance of spirochetes and resolution of symptoms even if administered after infection with *B.burgdorferi*.

pp; 51 DwgNo 0/4

7/3,AB/47 (Item 3 from file: 351)

DIALOG(R)File 351:Derwent WPI

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012470876

WPI Acc No: 1999-276984/199923

XRAM Acc No: C99-081276

New \*recombinant\*\* DNA vaccines lessening cholesterol ester transfer contain DNA encoding cholesterylester transfer protein

Patent Assignee: MONSANTO CO (MONS )

Inventor: GLENN K; NEEDLEMAN P

Number of Countries: 083 Number of Patents: 003

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 9915655	A1	19990401	WO 98US19366	A	19980917	199923 B
AU 9892317	A	19990412	AU 9892317	A	19980917	199934
EP 1015584	A1	20000705	EP 98944877	A	19980917	200035
			WO 98US19366	A	19980917	

Priority Applications (No Type Date): US 97934367 A 19970919

Patent Details:

Patent No	Kind	Lan Pg	Main IPC	Filing Notes
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WO 9915655 A1 E 98 C12N-015/12

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

AU 9892317 A C12N-015/12 Based on patent WO 9915655

EP 1015584 A1 E C12N-015/12 Based on patent WO 9915655

Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE

Abstract (Basic): WO 9915655 A1

Searcher : Shears 308-4994

**Abstract (Basic):**

NOVELTY - New recombinant DNA vaccines contain DNA encoding cholesteryl ester transfer protein, for producing antibodies to lessen the transfer of cholesteryl esters from HDL.

DETAILED DESCRIPTION - A novel process for producing antibodies to cholesteryl ester transfer protein (CETP) in a mammal comprises:

(a) immunizing the mammal with an inoculum containing a vehicle in which is dissolved or dispersed a recombinant DNA molecule comprising a DNA sequence that contains:

(i) a sequence encoding a CETP immunogen linked to;

(ii) a promoter sequence that controls the expression of the CETP immunogen DNA sequence in the mammal, the CETP immunogen being an immunogenic polypeptide having a CETP amino acid residue sequence, the immunization providing an amount of the recombinant DNA molecule to induce antibodies to CETP;

(b) maintaining the immunized mammal for the production of antibodies that bind to CETP.

INDEPENDENT CLAIMS are also included for:

(1) a process for increasing the concentration of high density lipoprotein (HDL) cholesterol in the blood of a mammal whose blood contains CETP comprising:

(a) step (a) as above;

(b) maintaining the immunized mammal for the CETP immunogen to be expressed and for the production of antibodies that bind to CETP and lessen the transfer of cholesteryl esters from HDL;

(2) an inoculum that comprises a recombinant DNA molecule comprising a DNA sequence that contains:

(1) a sequence encoding a CETP immunogen linked to;

(2) a promoter sequence that controls the expression of the CETP immunogen DNA sequence in a mammal, the recombinant DNA molecule being dissolved or dispersed in a vehicle.

USE - The method can provide an autogeneic immunological process for lessening the transfer of cholesteryl esters from HDL particles and for increasing the HDL cholesterol concentration of a mammal whose blood also contains CETP. The method may be useful in treating human pro-atherogenic dyslipoproteinemias characterized by low HDL/LDL cholesterol ratios.

ADVANTAGE - The method can have an effect that lasts for months as compared to the short-term effects of the small molecule drugs now available.

pp: 98 DwgNo 0/0

7/3,AB/48 (Item 4 from file: 351)

DIALOG(R) File 351:Derwent WPI

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012408958

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WPI Acc No: 1999-215066/199918

XRAM Acc No: C99-063399

Immunogenic \*fusion\*\*\* \*protein\*\*\* derived from \*group\*\*\* \*A\*\*\*  
\*streptococci\*\*\*

Patent Assignee: ID VACCINE (IDVA-N)

Inventor: DALE J B

Number of Countries: 079 Number of Patents: 003

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 9913084	A1	19990318	WO 98US19100	A	19980914	199918 B
AU 9893884	A	19990329	AU 9893884	A	19980914	199932
EP 1003875	A1	20000531	EP 98946991	A	19980914	200031
			WO 98US19100	A	19980914	

Priority Applications (No Type Date): US 9758635 A 19970912

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 9913084 A1 E 46 C12N-015/31

Designated States (National): AL AM AT AU BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

AU 9893884 A C12N-015/31 Based on patent WO 9913084

EP 1003875 A1 E C12N-015/31 Based on patent WO 9913084

Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

Abstract (Basic): WO 9913084 A1

Abstract (Basic):

NOVELTY - Immunogenic fusion polypeptide (I) that stimulates an immune response against group A streptococci (GAS) comprises:

(a) at least 2 peptides (Ia) from GAS, at least 10 amino acids long and able to induce a specific immune response and

(b) a peptide (Ib), C-terminal to (Ia) that protects the immunogenicity of the component described in (a) but is not essential for stimulation of the immune response.

DETAILED DESCRIPTION - DETAILED DISCLOSURE - An INDEPENDENT CLAIM is also included for a vaccine containing (I).

ACTIVITY - Antibacterial; Immunosuppressive.

MECHANISM OF ACTION - (I) induces a specific immune response (opsonising antibodies) against GAS. A hexavalent vaccine (based on Streptococcus pyogenes serotypes 1, 3, 5, 6, 19 and 24) was administered intramuscularly to mice (four doses; two of 25 mug and two of 50 mug, over 13 weeks), then the animals challenged with 20000 colony-forming units of serotype 24 cells. All 10 vaccinated animals survived, compared with only 1 of 10 non-vaccinated controls. The

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treatment also provided significant protection against challenge by serotype 24.

USE - Vaccines containing (I) are used to protect against GAS infections, specifically those caused by *Streptococcus pyogenes*, e.g. pharyngitis, pyoderma, toxic shock syndrome, deep tissue invasion, sepsis and acute rheumatic fever.

ADVANTAGE - (I) have improved immunogenicity and do not generate antibodies that are cross-reactive with human tissues.

pp; 46 DwgNo 0/7

7/3,AB/49 (Item 5 from file: 351)

DIALOG(R)File 351:Derwent WPI

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012313764

WPI Acc No: 1999-119870/199910

XRAM Acc No: C99-034899

XRXPX Acc No: N99-087512

Monoclonal antibody specific for E2A/pbx1 \*fusion\*\*\* \*protein\*\*\* - useful for diagnosis of acute lymphoblastic leukemia

Patent Assignee: PHARMINGEN (PHAR-N)

Inventor: GRUENWALD S; MONELL C; SANG B

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 5858682	A	19990112	US 96691997	A	19960802	199910 B

Priority Applications (No Type Date): US 96691997 A 19960802

Patent Details:

Patent No	Kind	Lan Pg	Main IPC	Filing Notes
US 5858682	A	21	G01N-033/567	

Abstract (Basic): US 5858682 A

The following are claimed: (1) a monoclonal antibody that specifically binds with an E2A/pbx1 fusion protein, where the antibody specifically binds to the fusion junction between E2A and pbx1 comprising the sequence SYSVLS and does not bind with the E2A peptide PDSYS; (2) a monoclonal antibody raised against an immunogenic fusion peptide comprising the sequence SYSVLS/YSVLS/SVLS (additional sequences may be present at the N-terminus of SYSVLS, except PD; (3) a hybridoma cell line that produces a monoclonal antibody as in (1); (4) a hybridoma cell line that produces a monoclonal antibody as in (2); (5) a monoclonal antibody that specifically binds with a splice-variant E2A/pbx1 fusion protein, raised against an immunogenic fusion peptide comprising the sequence PDSYSDESVRSPGTFLSIRGC; (6) a hybridoma cell line that produces a monoclonal antibody as in (5); (7) monoclonal antibodies or monoclonal antibody fragments produced using recombinant

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DNA techniques, which specifically bind with an E2A/pbx1 fusion protein, where the monoclonal antibody specifically binds to the fusion junction between E2A and pbx1 and does not bind with the E2A peptide PDSYS; (8) a monoclonal antibody which specifically binds to pbx1 protein and does not bind to pbx2 or pbx3 protein and which was raised against an immunogenic peptide containing a sequence that is not present in the pbx2 and pbx3 proteins; (9) a monoclonal antibody which specifically binds to pbx1 protein and does not bind to pbx2 or pbx3 protein and which was raised against an immunogenic peptide comprising three or more contiguous amino acids from the sequence ATNSAHGSQANSP; (10) a hybridoma cell line that produces a monoclonal antibody as in (8); (11) monoclonal antibodies or monoclonal antibody fragments produced using recombinant DNA techniques, which specifically bind pbx1 protein and not to pbx2 or pbx3 protein and which was raised against an immunogenic peptide containing sequence that is not present in the pbx2 and pbx3 proteins; and (12) a method for detecting a patient having acute lymphoblastic leukemia characterized by the presence of an E2A/pbx1 fusion protein.

USE - Useful for the diagnosis of acute lymphoblastic leukemia.

Dwg.0/2

7/3,AB/50 (Item 6 from file: 351)

DIALOG(R)File 351:Derwent WPI

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011293978

WPI Acc No: 1997-271883/199724

XRAM Acc No: C97-087424

New \*recombinant\*\*\* DNA for producing \*fusion\*\*\* \*proteins\*\*\* - comprising microbial pathogen epitope inserted into Haemophilus influenzae P2 \*protein\*\*\* loop 5, used in vaccine

Patent Assignee: UNIV NEW YORK STATE RES FOUND (UYNY )

Inventor: MURPHY T F; YI K; KYUNGCHEOL Y; TIMOTHY F M

Number of Countries: 020 Number of Patents: 002

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 9716207	A1	19970509	WO 96US17698	A	19961101	199724 B
US 6033877	A	20000307	US 956168	A	19951102	200019
			US 96740644	A	19961031	

Priority Applications (No Type Date): US 96740644 A 19961031; US 956168 A 19951102

Patent Details:

Patent No	Kind	Lan Pg	Main IPC	Filing Notes
WO 9716207	A1	E	54 A61K-039/102	

Designated States (National): CA JP

Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LU MC

Searcher : Shears 308-4994

NL PT SE  
 US 6033877 A C12N-015/31 Provisional application US 956168

**Abstract (Basic):** WO 9716207 A

A recombinant DNA molecule (I) is claimed, comprising a fusion sequence consisting of, and in frame for expression, a first nucleotide sequence encoding *Haemophilus influenzae* (HI) protein P2 with a second nucleotide sequence encoding one or more peptides which antigenically mimic epitopes from a microbial pathogen inserted within it, in place of a nucleic acid sequence encoding all or a portion of loop 5 amino acids. Also claimed are: (1) a recombinant vector comprising (I); (2) a host cell containing (I) or the recombinant vector as in (1); and (3) a fusion protein encoded by (I).

**USE** - The fusion proteins can be used as immunogens against disease caused by *Haemophilus influenzae* (HI) and/or the microbial pathogen. They can be used as immunogens in prophylactic and/or therapeutic vaccine formulations, or to generate specific antibody which may be useful for passive immunisation or as reagents for diagnostic assays. The fusion protein may especially be used to treat infection by respiratory pathogens, e.g. Group A *Streptococcus*, *Branhamella catarrhalis*, *Streptococcus pneumoniae*, *Bordetella pertussis*, *Pseudomonas aeruginosa*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, *Respiratory syncytial virus*, *Influenza virus*, *adenovirus*, *rhinovirus*, *Parainfluenza virus* and *Pneumocystis carinii* (not claimed).

**ADVANTAGE** - The recombinant DNA can provide for the production and delivery of biologically active, stable peptides. The peptides can be displayed as surface-exposed sequences.

Dwg.0/1

7/3,AB/51 (Item 7 from file: 351)  
 DIALOG(R) File 351:Derwent WPI  
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009658103  
 WPI Acc No: 1993-351655/199344  
 XRAM Acc No: C93-156084  
 XRPX Acc No: N93-271250

Synthetic peptide - comprises at least one B-cell epitope from \*streptococcal\*\*\* \*M\*\*\*-protein, useful in vaccine for streptococcal infections

Patent Assignee: COUNCIL QUEENSLAND INST MEDICAL RES (COUN-N)

Inventor: GOOD M F; PRUksAKORN S

Number of Countries: 022 Number of Patents: 002

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 9321220	A1	19931028	WO 93AU131	A	19930330	199344 B
AU 9337417	A	19931118	AU 9337417	A	19930330	199410

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Priority Applications (No Type Date): AU 921800 A 19920408

Patent Details:

Patent No	Kind	Lan Pg	Main IPC	Filing Notes
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WO 9321220	A1	E	57 C07K-007/08	
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Designated States (National): AU BR CA KR NZ US

Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT LU MC NL

PT SE

AU 9337417	A	C07K-007/08	Based on patent WO 9321220
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Abstract (Basic): WO 9321220 A

Synthetic peptide (A), comprising 1B-cell epitope from the C-terminus of M protein of Group A beta-haemolytic streptococci, is new. An antibody (Ab) reactive to B-cell epitope is only minimally reactive to human heart tissue. Also claimed are: (1) a vaccine for developing humoral immunity to M-protein, comprising (A); and (2) an Ab capable of binding to (A).

(A) pref. comprises 1 T-cell epitope from the C-terminus of M protein and/or from an extraneous part of, or fusion molecule with (A). (A) is produced by recombinant means or chemical synthesis. (A) comprises an N-terminal sequence derived from the conserved region of the M protein (i.e. residues 337-492 of type 5 M-protein) or single or multiple aminoacid substitutions, deletions and/or additions or chemical analogues. (A) pref. has the sequence L-R-R-D-L-D-A-S-R-E-A-K-K-Q-V-E-K-A-L-E. The T-cell epitope is from the C-terminus of M-protein or and extraneous part of, or fusion molecule with (A).

USE - (A) is useful, in a vaccine compsn., for immunising humans against streptococcal infections and the Ab is useful for diagnosing such infections.

Dwg.1a/3

7/3,AB/52 (Item 8 from file: 351)

DIALOG(R) File 351:Derwent WPI

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008864885

WPI Acc No: 1991-368910/199150

XRAM Acc No: C91-158973

New muscarinic receptor \*fusion\*\*\* \*proteins\*\*\* - obtd. by \*recombinant\*\*\* DNA techniques, used for producing antibodies and studying receptors

Patent Assignee: NAT INST OF HEALTH (USSH )

Inventor: BRANN M R; LEVEY A I; STORMANN T

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
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Searcher : Shears 308-4994

09/151409

US 7654971 A 19911112 US 91654971 A 19910214 199150 B

Priority Applications (No Type Date): US 91654971 A 19910214

Abstract (Basic): US 7654971 A

A recombinant DNA molecule (I) comprises: (a) a DNA segment which encodes a region of a cytoplasmic loop of a muscarinic receptor and (b) a vector for introducing the DNA segment into host cells; the muscarinic receptor cytoplasmic loop is present in a muscarinic receptor selected from M1, M2, M3, M4 and M5; the cytoplasmic loop is the inner third cytoplasmic loop of the receptor or i3.

Also claimed are a host cell (II) stably transformed or transfected with the recombinant DNA molecule as in (I) in a manner allowing expression of a protein encoded by the recombinant DNA molecule; recombinantly produced fusion protein(s) (III) consisting of a region of a muscarinic receptor cytoplasmic loop and an amino acid sequence encoded by a parent vector; and antibodies (IV) which are specific for the fusion proteins as in (III).

USE/ADVANTAGE - (III) can be used to produce antibodies which are specifically reactive with the muscarinic receptors M1-M5. (III) and (IV) are useful for studying the structure, function and localisation of the muscarinic receptor family in cells and tissues. The recombinant plasmids can also be used for making nucleic acid probes to specifically hybridise with the muscarinic receptor genes or mRNA.

(30pp Dwg.No.0/4)

7/3,AB/53 (Item 9 from file: 351)

DIALOG(R)File 351:Derwent WPI

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008718885

WPI Acc No: 1991-222904/199130

XRAM Acc No: C91-096853

New \*fusion"\*\* plasmid - for producing \*lipoprotein"\*\* signal \*peptide"\*\* fused to antigenic \*polypeptide"\*\*

Patent Assignee: NAT RES COUNCIL CANADA (CANA )

Inventor: LAU P; RIOUX C

Number of Countries: 018 Number of Patents: 004

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 9109952	A	19910711				199130 B
CA 2032914	A	19910627				199136
AU 9170346	A	19910724				199143
EP 510018	A1	19921028	WO 90CA460	A	19901227	199244
			EP 91901263	A	19901227	

Priority Applications (No Type Date): US 89456473 A 19891226

Searcher : Shears 308-4994

## Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 9109952 A

Designated States (National): AU JP US

Designated States (Regional): AT BE CH DE DK ES FR GB GR IT LU NL SE

EP 510018 A1 E 26 C12N-015/62 Based on patent WO 9109952

Designated States (Regional): AT BE CH DE DK ES FR GB GR IT LI LU NL SE

Abstract (Basic): WO 9109952 A

A fusion plasmid for in vivo synthesis of a lipid modified polypeptide, is new. The plasmid comprises a DNA sequence (I) encoding a lipoprotein signal peptide and at least the first amino acid of a mature lipoprotein. A DNA sequence (II) encoding a polypeptide is inserted into the plasmid to produce the lipid modified polypeptide. (I) encodes a lipoprotein signal peptide, cysteine and a sequence with a B-turn or exogenous protease recognition sequence. The signal peptide contains a positively charge N-terminal region, central hydrophobic region and C-terminal region comprising a recognition site for signal peptidase II. The recombinant fusion protein is also claimed.

USE/ADVANTAGE - The fusion plasmid allows for synthesis of immunogenic polypeptides as part of recombinant lipopeptides secreted across the cytoplasmic membrane and recovered from the cells.

In an example the expression of the lipid-modified peptide from plasmid pkLY4 was studied in the *C. coli* rec A lac Iq strain DH5aF'1Q. Compared to uninduced cells, transformants containing plasmid pkLY4 induced by IPTG synthesised an additional substance constituting the most abundant (3H)-palmitate -containing compound. (26pp Dwg.No.0/3)

7/3, AB/54 (Item 10 from file: 351)

DIALOG(R) File 351:Derwent WPI

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007367952

WPI Acc No: 1988-001887/198801

XRAM Acc No: C88-000866

\*Recombinant\*\*\* DNA encoding \*fusion\*\*\* \*protein\*\*\* of Newcastle disease virus - or its \*immunogenic\*\*\* \*polypeptide\*\*\* fragments, useful in poultry vaccine

Patent Assignee: SMITH KLINE RIT SA (SMIK )

Inventor: BURNY A; DEBOUCK C; ESPION D

Number of Countries: 018 Number of Patents: 006

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
EP 252060	A	19880107	EP 87870091	A	19870629	198801 B
AU 8774920	A	19880107				198810
JP 63024888	A	19880202	JP 87165127	A	19870629	198810
DK 8703359	A	19871231				198819

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PT 85220 A 19880701 198831  
ZA 8704677 A 19881130 ZA 874677 A 19870629 198901

Priority Applications (No Type Date): US 86880371 A 19860630

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes  
EP 252060 A F 21

Designated States (Regional): AT BE CH DE ES FR GB GR IT LI LU NL SE

Abstract (Basic): EP 252060 A

New recombinant DNA molecule (I) comprises a sequence coding for the fusion protein of newcastle disease virus (NDV) or a fragment or deriv. of this coding for a polypeptide able to induce an immune response to the fusion protein. Also new are (1) a 1764 base-DNA sequence (reproduced with corresponding amino acid sequence in the specification) coding for NDV fusion protein; (2) vectors for expressing this DNA when inserted downstream of a regulatory region in yeast and (3) microorganisms transformed with this DNA.

USE/ADVANTAGE - NDV fusion protein, and immunogenic polypeptides, are useful in vaccines for protecting poultry against NDV infection and can also be used diagnostically. Such vaccines, unlike those based on attenuated viruses, can be used without risk of inducing respiratory disorder.

In an example, the multi copy shuttle vector pCD192 was digested with PvoII and ligated with a fragment isolated from II.14(F) by digestion with BamHI and FspI to form the specifically claimed vector PYDE1. This was used to transform the yeast strain BR10 and translation (controlled by the Cu-Mt promoter) induced in presence of 0.1 mM CuSO4. Proteins were sepd. by electrophoresis and examined for ability to react with polyclonal anti-NDV antibody Western blot analysis showed that in yeast the fusion protein was produced in 2 forms of slightly different mol. wts.

Set	Items	Description	Author
S8	11	AU=(DALE, J? OR DALE J?) AND S3	
S9	7	S8 NOT S	
S10	3	S8 NOT S6	
S11	3	RD (unique items)	

>>>No matching display code(s) found in file(s): 65, 113

11/3,AB/1 (Item 1 from file: 144)  
DIALOG(R)File 144:Pascal  
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13963849 PASCAL No.: 99-0145910  
Multivalent \*group\*\*\* \*A\*\*\* \*streptococcal\*\*\* vaccine designed to  
optimize the immunogenicity of six tandem M protein fragments  
\*DALE J B\*\*\*

Veterans Affairs Research Service and the Department of Medicine,  
University of Tennessee, Memphis, TN 38104, United States

Journal: Vaccine, 1999, 17 (2) 193-200

Language: English

One of the major challenges in the development of \*group"\*\* A \*streptococcal"\*\* \*M"\*\* protein-based vaccines is the multiplicity of M types expressed by these organisms. Previous studies have shown that multivalent vaccines containing as many as eight M protein fragments in tandem were immunogenic and evoked opsonic antibodies. It was also noted that the C-terminal fragments of these hybrid proteins were often not immunogenic or evoked only low levels of opsonic antibodies suggesting that the C-terminus of the molecule may have been preferentially degraded or altered in vivo. In the present studies, we designed a hexavalent vaccine containing protective M protein peptides from types 24, 5, 6, 19, 1, and 3 \*group"\*\* \*A"\*\* \*streptococci"\*\*. In order to "protect" the carboxy-terminal components, the amino-terminal \*M24"\*\* fragment was reiterated on the carboxy-terminal end of the construct. The hexavalent vaccine was immunogenic in laboratory animals and evoked high titers of antibodies against each of the native M proteins represented in the vaccine and bactericidal antibodies against all six serotypes of \*group"\*\* \*A"\*\* \*streptococci"\*\*. The vaccine was equally immunogenic when delivered in alum or in complete Freund's adjuvant. None of the immune sera contained antibodies that crossreacted with human heart tissue. Our results show that complex multivalent \*group"\*\* \*A"\*\* \*streptococcal"\*\* vaccines can be designed in such a way that each M protein fragment is immunogenic and evokes protective antibodies.

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11/3,AB/2 (Item 1 from file: 357)  
DIALOG(R)File 357:Derwent Biotechnology Abs  
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0236662 DBA Accession No.: 99-06763 PATENT  
Immunogenic \*fusion"\*\* \*protein"\*\* derived from \*group"\*\*-\*A"\*\* \*streptococci"\*\* - used in infection vaccine or nucleic acid vaccine  
AUTHOR: \*Dale J B"\*\*  
CORPORATE SOURCE: Bothell, WA, USA.  
PATENT ASSIGNEE: ID-Vaccine 1999  
PATENT NUMBER: WO 9913084 PATENT DATE: 990318 WPI ACCESSION NO.:  
99-215066 (9918)  
PRIORITY APPLIC. NO.: US 58635 APPLIC. DATE: 970912  
NATIONAL APPLIC. NO.: WO 98US19100 APPLIC. DATE: 980914  
LANGUAGE: English  
ABSTRACT: A new immunogenic \*fusion"\*\* \*protein"\*\* that stimulates an immune response against \*group"\*\*-\*A"\*\* \*streptococci"\*\* (GAS) consists of at least 2 \*peptides"\*\* from GAS, at least 10 amino acids in length

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and able to induce a specific immune response, and a \*peptide\*\*\* (C-terminal to the GAS \*peptides\*\*\*), that protects the immunogenicity of the GAS \*peptides\*\*\* but is not essential for stimulation of the immune response. Also claimed is a vaccine containing the \*fusion\*\*\* \*protein\*\*\*, used to protect against GAS infections, specifically those caused by Streptococcus pyogenes involved in pharyngitis, pyoderma, toxic shock syndrome, deep tissue invasion, sepsis and acute rheumatic fever. Also disclosed is the use of the DNA in a nucleic acid vaccine. (46pp)

11/3,AB/3 (Item 1 from file: 351)  
DIALOG(R)File 351:Derwent WPI  
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013270769  
WPI Acc No: 2000-442675/200038  
XRAM Acc No: C00-134759

New Spa polypeptides and polynucleotides isolated from a Streptococcus species, useful for eliciting opsonic antibodies in an animal that are protective against Streptococci infections

Patent Assignee: UNIV TENNESSEE RES CORP (UYTE-N)

Inventor: \*DALE J\*\*\*

Number of Countries: 090 Number of Patents: 002

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200037648	A1	20000629	WO 99US30807	A	19991222	200038 B
AU 200023846	A	20000712	AU 200023846	A	19991222	200048

Priority Applications (No Type Date): US 98114730 A 19981231; US 98113794 A 19981222

Patent Details:

Patent No	Kind	Lan Pg	Main IPC	Filing Notes
WO 200037648	A1	E	85 C12N-015/31	

Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

AU 200023846 A C12N-015/31 Based on patent WO 200037648

Abstract (Basic): WO 200037648 A1

Abstract (Basic):

NOVELTY - A Spa polypeptide (I) isolated from a Streptococcus species is new and comprises a polypeptide having at least 50% amino acid sequence identity to sequences (2) (a 112 amino acid residue sequence, fully defined in the specification) or sequence (5) (a

sequence not defined in the specification).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) (I) comprising the amino acid sequence (2) or (5) or variants which include amino acid sequences having conservative amino acid substitutions or have at least 90% sequence identity to (2) or (5);
- (2) a peptide (I') comprising at least 23 amino acids of the N-terminus of (I);
- (3) an immunogen for protecting an animal against a streptococcus infection comprising (I) or (I') (or at least a peptide comprising at least 8 contiguous amino acids from the peptide);
- (4) an antibody that specifically binds to an epitope present on (I) or (I');
- (5) an isolated nucleic acid molecule (II) comprising sequences (1) (not defined in the specification) or (4) (a 1872 base pair sequence fully defined in the specification) or a sequence that encodes (I) or a complement of the nucleic acid molecule;
- (6) an isolated nucleic acid molecule (II') comprising a sequence comprising sequences (1) or (4), a complement or variants which are selected from sequences that encode the polypeptide (2) or (5) which are degenerate to (1) or (4) because of the genetic code, sequences that encode a polypeptide which have conservative amino acid substitutions to the polypeptide of (2) or (5) or sequences that encode a polypeptide that is at least 50% identical to (2) or (5);
- (7) an isolated nucleic acid molecule (II'') comprising a sequence that hybridizes to (II') under conditions of moderate stringency;
- (8) an isolated nucleic acid molecule (II''') comprising a sequence that encodes an opsonic epitope from a Spa polypeptide comprising a polypeptide having at least 50% amino acid sequence identity to (2) or (5);
- (9) a vector (III) comprising the isolated nucleic acid molecule (II)-(II''') operably linked to a promoter where the vector expresses a polypeptide encoded by the isolated nucleic acid when the vector is introduced into a host cell;
- (10) a host cell (IV) carrying (III);
- (11) a therapeutic composition for protecting an animal from a streptococcus infection comprising a biologically acceptable diluent and an effective amount of an immunizing agent selected from:
  - (a) a Spa polypeptide isolated from Streptococcus comprising a polypeptide having at least 50% amino acid sequence identity to (2) or (5);
  - (b) an immunogen comprising an opsonic epitope obtained from (I);
  - (c) a host cell that expresses an opsonic epitope obtained from (I); or
  - (d) an antibody that specifically binds to (I); and
- (12) a therapeutic method for protecting an animal against a Streptococcus infection comprising administering to the animal the therapeutic composition where administering the therapeutic composition

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elicits opsonic antibodies in the animal.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Immunostimulant.

USE - The polypeptides, nucleic acid molecules and antibodies are useful for protecting an animal against a Streptococcus infection in humans.

ADVANTAGE - No advantages stated in the specification.

pp; 85 DwgNo 0/7

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